September 6, 2000

Note to the Reader:

This document, entitled *An SAB Report on Certain Elements of the Proposed Arsenic Drinking Water Regulation*, was developed by the Drinking Water Committee (DWC) of the US EPA Science Advisory Board (SAB). This report is now being sent to the SAB Executive Committee for review and approval. Following the Executive Committee's review, the report will become final and will be transmitted to the Administrator.

This draft report is also being released for general information to members of the public and to Agency staff. This is consistent with the SAB policy of releasing draft materials when the reviewing committee has reached consensus on the contents, and the document is sufficiently complete to provide useful information to the reader. Pending Executive Committee approval, the draft document should not be used to represent official Agency or SAB views or advice. Draft documents at this stage of the process often undergo revisions before the final version is approved and published.

The SAB is not soliciting comments on the advice contained herein. However, as a courtesy to the Agency offices and laboratories associated with the subject of this SAB review, we will receive and consider pertinent comments on whether:

1) the Committee adequately responded to the questions posed in the charge?

2) any statements or responses in the draft document are not clear?

3) there are any technical errors in the draft document?

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The Honorable Carol Browner
Administrator
United States Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Subject: An SAB Report on Certain Elements of the Proposed Arsenic Drinking Water Regulation

Dear Ms. Browner:

This Report was developed by the Drinking Water Committee (DWC) of the Science Advisory Board (SAB) in response to interactions with the Agency's Office of Water and Ground Water during the June 2000 and August 2000 DWC meetings.

The principal issue before the DWC was consideration of the proposed reduction of the MCL for arsenic in drinking water from 50 to 5 μg/L. The DWC commends the Agency for undertaking this proposal as it has been clear for some time that reconsideration of the arsenic MCL was in order. While the Committee recognized the need for reduction in the MCL, there was some diversity of opinion as to the level that would be most appropriate.

The DWC has spoken to some of the issues that make reduction of the MCL to 3 or 5 μg/L (the proposed MCL) difficult. The majority of members did feel that there was adequate basis for the Agency to consider use of its discretionary authority under the 1996 Amendments to the Safe Drinking Water Act to consider higher MCLs (i.e. greater than 5 μg/L). In the opinion of the DWC, the Agency has misinterpreted some of the conclusions of the National Research Council's arsenic report (NRC, 1999). First EPA accepted, as a risk assessment itself, what was meant as an exercise to determine if available human data were sufficiently detailed that modeling of risk could be accomplished. As indicated by the Academy, this was not meant to substitute for further analyses of most appropriate methods that should have been explored by the Agency. As NRC (1999) noted, there are several reasons why the Taiwanese data should not be accepted as being directly applicable to the U.S. In particular, NRC identified clear deficiencies in selenium intake in the population as well as other nutritional analyses and the socioeconomic differences between the study area and the rest of Taiwan. Further analyses of the Taiwanese data have been performed since the NRC report was issued that bring into serious question the use of the comparison populations outside the study area for estimating

cancer risks due to arsenic. A study in Utah suggests that some U.S. populations may be less susceptible to the development of cancer, although the Committee found that study difficult to use in a quantitative way because of the manner in which the data were presented. Finally, as pointed out by the NRC (1999), the mechanisms associated with arsenic induced cancer have a sublinear character which implies that linear models overestimate the risk. Thus, the DWC recommends that in future considerations of the arsenic MCL, the Agency more thoroughly explore the risks associated with arsenic utilizing alternative models and considering the probable differences between the Taiwanese study populations and U.S. populations via a formal risk assessment. This should also consider the factors affecting susceptibility of the developing fetus and children to arsenic.

Further analyses of the Taiwanese data now available to the DWC (Morales, et al., 2000), but not to the NRC (see NRC, 1999) point out that the incremental increases in lung cancer and bladder cancer associated with arsenic exposure were of roughly the same magnitude rather than EPA's estimated 2 - 5 times higher rates for lung cancer relative to bladder cancer.

The DWC also has some reservations related to the Agency's cost projections for the arsenic rule. In part, this was because of differences between the Agency projections and those of other organizations (i.e. AWWARF. 2000). However, there were several assumptions made in EPA's analysis relative to the disposal of arsenic residuals that the DWC felt were not realistic. The DWC feels that assuming that high-salt residuals can be disposed of through POTWs is unrealistic. In addition, the assumption that solid residuals can be disposed in municipal landfills as a non-hazardous waste is flawed. In this regard, the Agency also assumed that a 10-fold reduction of the arsenic MCL would have no effect on the levels of arsenic necessary to classify a treatment residual as being non-hazardous by other programs of the Agency.

Another problem is that while many of the treatment options identified as best available technology (BAT) are fairly standard in drinking water treatment, they have not been applied or optimized for arsenic removal at a large scale. The behavior of arsenic is fairly unusual and it is not clear that these technologies can be simultaneously operated efficiently for arsenic removal and for their other intended purposes.

The Committee suggested that there should be some further review of the concept of affordability as it is applied to new MCLs. There is some question about whether the $750 estimate for national median household income used by EPA is appropriate for the small systems that will largely be the impacted systems for the arsenic rule. In addition, the Agency needs to evaluate cumulative costs of multiple rules, because each new rule adds some incremental cost to the overall cost of drinking water to specific households. It also provided some discussion of whether the practical quantitation limit (PQL) for arsenic was really as low as 3 µg/L. Finally, a suggestion was made that the Agency might profitably consider the development of a phased rule largely based on the uncertainties in cost

projections, but also with some consideration of the uncertainties articulated regarding the levels that give rise to adverse health effects.

Thank you for the opportunity to review these elements of the arsenic proposal. We would be happy to continue to engage with EPA as it pursues this action. We look forward to your response to this report.

Sincerely,
Dr. .....

NOTICE

This report has been written as part of the activities of the Science Advisory Board, a public advisory group providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide balanced, expert assessment of scientific matters related to problems facing the Agency. This report has not been reviewed for approval by the Agency and, hence, the contents of this report do not necessarily represent the views and policies of the Environmental Protection Agency, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names or commercial products constitute a recommendation for use.

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U.S. Environmental Protection Agency
Science Advisory Board
Drinking Water Committee
Arsenic Review Panel

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A SCIENCE ADVISORY BOARD/DRINKING WATER COMMITTEE REVIEW OF CERTAIN ELEMENTS OF THE PROPOSED ARSENIC DRINKING WATER REGULATION

1. EXECUTIVE SUMMARY

The Drinking Water Committee (DWC) met from June 5 - 7, 2000 and again on August 8, 2000 to consider components of the Agency's proposal of a new MCL for arsenic in drinking water. The established MCL is 50 μg/L. The current rule proposes to lower the MCL to 5 μg/L and requests comments on alternatives of 3, 10 and 20 μg/L. The lowering of a national standard by a factor of ten is obviously a major change that will have significant cost impacts for compliance. In the case of arsenic, the costs involved are substantial, but somewhat problematic because it demands a level of treatment not ordinarily utilized in the small systems that are principally the focus of the rule.

The major background document on arsenic's health effects that was provided to the DWC was the 1999 National Research Council's report on arsenic in drinking water (NRC, 1999). The committee reviewed this and additional material that it identified in order to answer the charges related to the forms of arsenic that are responsible for the adverse effects and the influence of dietary arsenic sources on the risks projected from the arsenic studies conducted in Taiwan. The DWC also responded to specific EPA questions about the necessity of issuing an advisory to mothers of young children who may be using tap water for the preparation of infant formula. The DWC also chose to comment on the Agency's use of the information provided by the NRC (1999) report. In particular, the committee examined whether the Agency appropriately responded to the substance of the report in developing their regulatory options.

In general, the DWC found that determining the forms of arsenic responsible for producing adverse effects has become more complex since the publication of the NRC report. It can no longer be concluded that inorganic forms are the only active forms responsible for the carcinogenic effects associated with arsenic. However, the committee agrees that because arsenic in drinking water is largely of the inorganic form, that those are the appropriate forms for EPA's regulatory focus. Recent findings have also complicated comparisons of the relative importance of food and water sources of arsenic. As long as the agency resorts to linear extrapolations of arsenic's cancer risk, these problems can be minimized by simply considering drinking water arsenic as an incremental risk superimposed on a more complex background of arsenic in food. The Committee concluded that based on present information, reducing drinking water arsenic exposure to levels below that in food rapidly reaches a point of greatly diminished returns in terms of health benefits.

The DWC had a strongly mixed reaction to the issuance of an advisory to mothers with young infants. While most panelists thought an advisory was potentially valuable, the lack of a clear description from EPA on what an advisory would contain or how it would be implemented kept them from fully endorsing an Advisory. The Committee noted that the release of a Health Advisory was an EPA policy decision. The Committee noted further that the advisory discussed by EPA did not appear to be the same as past drinking water Health Advisories, therefore, special consideration may be necessary. The main concerns expressed by the committee focused on possible unanticipated consequences of an advisory. If EPA chooses to issue an advisory, the Committee advises caution and recommends that EPA follow techniques that come in large part from good practices in the pediatric and public health communities. Considerable attention must be given to how and to whom the advisory should be issued. While the committee had mixed opinions on the value of such an advisory, there was unanimous agreement that it should not be simply issued to mothers through the normal methods for public notification of problems in drinking water.

The DWC commented extensively on the Agency's interpretation of the National Research Council's arsenic report. The DWC believes that the Agency took the modeling activity of the NRC report as being prescriptive despite the clearly stated intention in the report that their efforts were only examples, not actual risk assessments. The Committee also addressed with some complex issues about the nutritional status of the Taiwanese population that formed the basis of the NRC examples and the need to consider lung cancer risk in the final risk assessment. Analyses available since the NRC report led the committee to conclude that the contribution of lung cancer to overall risk is about the same as that of arsenic's bladder cancer risks. The DWC also reemphasized the NRC's cautions about selenium status and other nutritional and socioeconomic factors that likely make the studied Taiwanese population more sensitive than would be anticipated in the general the U.S. population.

The DWC notes that the Agency should have thoroughly explored arsenic's potential risks in a formal risk assessment. This should include modeling of the factors noted above that are important to arsenic toxicity and which vary across populations. Such a risk assessment should also recognize the tenet that children are not young adults; differences in diet, metabolism, body weight, variable age groups, consumption of water, toxic effects of metal pollutants in a rapidly growing organism, and exposure estimates per unit of body weight should be essential considerations in a risk assessment of children.

Attachment A to this report, entitled *A Minority Report on Arsenic in Drinking Water: The Unique susceptibility of Children to Arsenic*, by Dr. John Rosen, a consultant to the DWC for the arsenic review, provides an analysis of issues relative to the differential sensitivity of children to arsenic that departs from the majority opinion contained in this report. Dr. Rosen is joined in this dissenting view by Dr. Barbara Harper a member of the Drinking Water Committee.

The Agency also directed questions to the DWC on the cost of compliance with the proposed rule, with particular attention directed at disposal options for brines and other residuals from treatment and factors used in the selection of alternative treatment technologies. In addition to these specific charge questions, the DWC chose to comment on the Agency's National Affordability Criteria, especially their application to small communities, and the practical quantitation limits (PQL) for arsenic in water.

The committee agrees that EPA has covered the spectrum of residual disposal alternatives. However, the committee feels that certain alternatives are not viable due to potential constraints placed on utilities. It is the consensus of the committee that disposal of high-TDS brines to a publicly owned treatment work (POTW) will not be viable due to regulatory limits on TDS and dilution of organic wastes in the majority of systems.

Generally, the committee believes that the costs estimated by EPA for the rule appear to be low. From the limited information provided and from EPA's presentations to the committee at its June, 2000 meeting, the model appears to have certain deterministic and probabilistic components that make it very complex. The Committee questions whether the technologies identified as best available technologies (BAT) are appropriately considered as such because most of them have not been implemented or optimized for arsenic removal at large-scale. If optimization of these technologies for arsenic removal reduces their effectiveness for the purposes for which they have been designed, there could be substantial underestimates of the costs of compliance. Largely because of these issues, and recognizing that this is a policy call to be made by EPA, the Committee suggests that the Agency might consider a phased rule.

The National Affordability Criteria concerned the Committee as well. First, the communities impacted may well be below the National Median Income, which means that the proportion of their income required will be significantly greater than that estimated by the Agency. Second, the Agency documentation did not explicitly show an examination of incremental costs associated with other rules that could impact these systems at the same time. Concern was also expressed over the possibility of some unintended consequences (e.g. abandonment of some of the small community water systems).

The Committee also questioned whether the PQL had been established in natural waters. Some data were supplied to indicate that the currently considered PQL of 3 µg/L may be significantly higher when measured in natural waters.

Despite the uncertainties in the risk assessment for arsenic, there seems to be a growing consensus among those familiar with the arsenic issue for a substantial reduction in the current MCL for arsenic. The SAB's DWC is unanimous in its support of a reduction, though individual members of the DWC vary considerably on where they believe the actual MCL should be set. Some members of the

Panel suggest that the Agency might want to consider the development of a phased rule, largely to resolve questions relative to the effectiveness and cost of compliance. Initially setting a higher MCL would require treatment by a representative number of community water systems. The experience gained from this effort would then provide needed data to actually plan for the much larger number of systems that would be required to treat to a lower MCL that would be identified as the ultimate target.

2. INTRODUCTION AND CHARGE

2.1 Introduction

EPA's Office of Ground Water and Drinking Water (OGWDW) proposed a new Maximum Contaminant Level (MCL) for arsenic of 5 μg/L on June 22, 2000 (EPA, 2000). This is a substantial change from the current MCL of 50 μg/L. The existing MCL was based on concerns related to arsenic carcinogenicity with a primary focus on skin cancer. In considering the revision of the MCL, new data on several issues were considered. These included:

a) The quality of the available epidemiological data;
b) Consideration of internal cancers and other health effects attributed to arsenic in continuing analyses of the data from Taiwan and other populations having drinking water with elevated arsenic levels;
c) The applicability of the data from Taiwan to the U.S. population;
d) Whether the mechanisms involved require linear or non-linear risk extrapolation; and
e) Practical limitations on the measurements of low levels of arsenic in drinking water.

Since the arsenic MCL was last considered, there have been new analyses conducted on the available epidemiological data (some new studies have at least qualitatively supported the findings in Taiwan), and the focus of the analyses have turned from skin cancer to internal cancers, particularly cancers of the bladder and lung (NRC, 1999). There are now data that allow us to begin to consider whether risk extrapolation for low doses should be linear or non-linear. However, studies now suggest that the mechanisms involved in arsenic-induced cancer are more complex than previously recognized. This led the NRC to conclude that although there are data that support non-linear risk extrapolation, the data are not sufficiently clear for identifying a point of departure based on alternative modes of action. Finally, there are now data that support much lower practical quantitation limits for arsenic in drinking water.

2.2 Charge

The Agency charge to the Drinking Water Committee concerned both health effects and treatment technology issues. The specific questions from EPA are shown below.

2.2.1 Arsenic Health Effects Charge to the SAB

Charge Question 1: **Concentration on inorganic arsenic as principal form causing health effects.** EPA has identified inorganic arsenic as the principal form causing health effects, and the literature indicates that most arsenic in drinking water is inorganic. EPA's MCLG and MCL do not distinguish between arsenate and arsenite. Does the SAB have perspectives on this issue that it believes EPA should consider in developing its risk assessment?

Charge Question 2: **Implications of natural arsenic exposure through food.** The 1999 NRC report estimated the daily inorganic food intake by assuming that 10% of the arsenic in seafood is inorganic, and all other foods are 100% inorganic arsenic. NRC noted that these assumptions set an upper bound on the contribution from food, which is about 10 µg a day for adults. Does SAB agree with the implied NRC perspective that relative source contribution of food should be taken into consideration in the setting of the drinking water standard and how might we consider this and communicate it to the public?

Charge Question 3: **Health Advisory on low arsenic water and infant formula.** The NRC report was inconclusive about the health risks to the pregnant woman, developing fetus, infants, lactating women, and children. Given the potential for cardiovascular disease (as evidenced by EPA's Utah studies and extensive other data) and uncertainty about risks to infants, EPA plans to issue a health advisory to recommend use of low-arsenic water in preparation of infant formula. Is this precautionary advice appropriate given the available information?

2.2.2 Arsenic Treatment Charge to the SAB

Charge Question 4: Decision tree for waste disposal options for arsenic treatment brines and spent media. EPA identified waste disposal options that will likely be used for arsenic treatment residuals. EPA assigned national selection probabilities to each of option in a decision tree. Some people are concerned that after the drinking water MCL is lowered, the Toxicity Characteristic for arsenic will be lowered and that many drinking water treatment residuals will be subject to the costly hazardous waste management regulations. EPA believes that its analysis shows that residuals should be nonhazardous, under the current TC of 5 mg/L and even if the TC

were revised to 0.5 mg/L. EPA suggests that important questions relating to waste disposal do not relate to hazardous waste disposal. Rather, for brines, they relate to questions such as TDS (total dissolved solids) restrictions in waters receiving brine, and restrictions on sanitary sewer discharge due to TBLLs (technically based local limits). For sludge disposal, they relate to restrictions that may be placed on land application, which may result in more systems using landfills.

Based upon a review of the attached materials, does the SAB believe that the EPA produced an accurate projection of the likely disposal options for arsenic residuals and the distribution of these options by treatment type? What are the SAB's views on the advantages and the limitations of the various waste disposal options? What effect, if any, would the SAB's analysis of these advantages and limitations have on the probabilities assigned? What are the SAB's views on which options will be more likely used by small systems (less than 10,000 people), and which will be more likely used by larger ones?

Charge Question 5: **Decision tree for ground water treatment technologies.** EPA has identified treatment technologies that will likely be used to treat arsenic in groundwater systems. These include ion exchange, activated alumina, reverse osmosis, coagulation-assisted microfiltration, greensand filtration, and point-of-use and point-of-entry devices. The EPA has also identified non-treatment options such as regionalization and alternate source. EPA consulted with small utilities and AWWA in order to identify issues which would affect selection of treatment technologies for small systems, which included cost, complexity of operation, chemical handling issues, and frequency of maintenance on point-of-use devices. EPA has assigned selection probabilities to each of these options in a decision tree that form the basis for the Agency's overall cost projections. The portions of the preamble that explain this decision tree as well as certain other relevant documents are attached.

Does the SAB agree with the principal "branches" of EPA's decision tree described in the attached documents and the likelihood that these options will be used for systems of various sizes with various source water characteristics? What views does the SAB have on EPA's description of the advantages and limitations of these treatment technologies? Would the SAB's views on the these advantages and limitations affect the probabilities assigned?

3. HEALTH EFFECTS ISSUES

3.1 Comments on the Evaluation of Health Effects and Risk Issues

3.1.1 Charge Question 1. Inorganic arsenic as the principal form causing health effects.

EPA has identified inorganic arsenic as the principal form causing health effects, and the literature indicates that most arsenic in drinking water is inorganic. EPA's MCLG and MCL do not distinguish between arsenate and arsenite. Does the SAB have perspectives on this issue that it believes EPA should consider in developing its risk assessment?

The principal form of arsenic responsible for causing health effects is not clear from the available literature. Studies available since the NRC (1999) report indicate that organic arsenicals are of interest as carcinogens (Wei et al., 1999; Arnold et al., 1999). In addition, the +3 valence state of monomethyl arsenic was found to be much more cytotoxic than inorganic forms (Petrick et al., 2000). On the one hand, methylation aids in the elimination of arsenic from the body, but on the other, it appears that it may generate chemical species that are responsible for adverse effects in some target organs or cells (Aposhian et al., 1999).

A carcinogenic effect has been observed in the bladder of rats administered DMA for their lifetime (Wei et al., 1999). These studies did not detect an increased incidence of urinary bladder tumors at 12.5 mg/L administered in the water; however, an increase was observed at doses of 50 and 200 mg/L DMA. Further, studies by Arnold et al. (1999) indicated a lack of a carcinogenic response to DMA in mice at concentrations of up to 100 mg/kg in the diet indicating that mice are resistant to bladder carcinogenesis by arsenic. However, Arnold, et al., (1999) confirmed that at 40 and 100 mg/kg DMA in the diet proved carcinogenic to the uroepithelium, while 2 and 10 mg/kg did not. The carcinogenic action is greater in female than male rats and is dose responsive at 40 and 100 mg/kg in female rats. In female rats exposed to DMA at 40 and 100 mg/kg in the diet, cytotoxicity was observed in the urinary bladder epithelium. These are the only animal studies performed in the absence of a co-carcinogen that demonstrates an induction of bladder cancer by arsenic or one of its metabolites when administered chronically. The doses of arsenic required are very high levels compared to the amount of DMA expected to be formed following ingestion of inorganic arsenic in drinking water. As a result these data point to the potential that another form(s) of arsenic is responsible. However, it is improbable that this carcinogenic result would be explained by conversion of DMA to inorganic arsenic (Carter et al., 1999).

The DWC recommends that further refinements of the risk assessment for arsenic focus on the concentrations of various arsenic metabolites in the urine, the serum, and uroepithelial cells of rats treated with these same doses of DMA. This exercise would establish the relationship between bladder

carcinogenesis and urine concentration and speciation of arsenic. This could be used to predict the concentrations of these arsenic metabolites that would be produced following exposure to inorganic forms of arsenic. In turn, this would inform the Agency on the intake of inorganic arsenic needed to produce carcinogenic concentrations of specific arsenic metabolites in the human bladder under a variety of different exposures. These models should consider the bladder as a reservoir for arsenic with the concentration varying over the course of the day.

This does not suggest that inorganic arsenic cannot also play a role in other target organs. Ng et al., (1999) found increased incidences of tumors in the lung and gastrointestinal tract when sodium arsenate was administered at 0.5 mg As/L in drinking water to female C57Bl/6J mice (corresponding to 67 μg/kg body weight per day). Lung cancer is also implicated in the human population exposed to arsenic (NRC, 1999). The varying responses of different test animals can reflect differences in genetic susceptibility. However, it is also consistent with the possibility that the development of tumors in different tissues could result from different metabolites or metabolite combinations.

Adding to the complexity, are recent findings that a +3 valence state of organic arsenic is much more toxic to cells in culture than the +5 organic forms that have been previously studied. Petrick et al.. (2000) found that monomethylarsonous acid, a +3 valence form of organic arsenic, is much more cytotoxic to cells in culture than inorganic forms of arsenic, as well as the +5 forms of methylated arsenic. Styblo et al. (1999, 2000) have very similar findings in cultures of rat hepatocytes and human cells derived from the liver, skin, urinary bladder, and cervix with the +3 form of DMA as well as MMA. These forms of arsenic are likely to be a short-lived intermediates *in vivo*, and as a consequence would be found only at low concentrations compared to the +5 forms. At any rate, it is no longer clear that the inorganic forms are the most toxic either (as opposed to being carcinogenic). Consequently, in the future, it will be much more important to specify the dose, endpoint and target organ when speaking of arsenic's toxicity, because the form responsible may well vary. Therefore, it is probable that human responses are determined by a variety of conditions and may involve interactions between metabolites.

Although there are exceptions, the principal forms of arsenic in drinking water are inorganic forms, and the Agency is setting standards for arsenic as it appears in drinking water. Because the Agency has chosen to adopt the linear model used for illustrative purposes in the NRC (1999) report, it would be best to simply deal with the incremental risk of arsenic in drinking water. For this reason alone, the Agency needs to focus on the inorganic forms of arsenic rather than attempting to deal with all potential forms of arsenic. Essentially, it is not possible to consider contributions of different forms of arsenic to the overall response based on the data that is available today. This conclusion makes it very difficult to make recommendations on the comparative risks of arsenic in food vs. water with any confidence.

3.1.2 Charge Question 2: Implications of natural arsenic exposure through food. The 1999 NRC report estimated the daily inorganic food intake by assuming that 10% of the arsenic in seafood is inorganic, and all other foods are 100% inorganic arsenic. NRC noted that these assumptions set an upper bound on the contribution from food, which is about 10 µg a day for adults. Does SAB agree with the implied NRC perspective that relative source contribution of food should be taken into consideration in the setting of the drinking water standard and how might we consider this and communicate it to the public?

The consideration of relative source contribution to the total arsenic intake places drinking water exposure into a practical context. Ideally, a source of a chemical that exists in many forms would be weighted by the potency of the form of chemical that is present in producing the effect of interest. The likely involvement of organic forms of arsenic in the induction of bladder and lung cancers, based on animal data complicates the picture, because the assumption prior to the development of these data was that only inorganic arsenic forms were responsible. Inorganic forms of arsenic cannot be involved in the induction of cancer by DMA because it is not demethylated *in vivo*. There are no data for comparison of the potency of the various forms of arsenic. Neither the NRC nor EPA considered the kinetics of their formation. Therefore, the DWC can only comment that the lack of data increases the uncertainty about the relative contribution of drinking water to cancer induced by arsenic relative to that in food.

To remain within the context of the framework used by NRC and EPA, the DWC first addressed the above charge to examine the ranges of arsenic exposure through food and water separately and then explored the relative contributions of food under various concentrations of arsenic in drinking water. Accepting that inorganic arsenic is the major concern in drinking water, the DWC determined how arsenic exposures via these two pathways would contribute to produce adverse human health effects. The Committee found that this depends entirely upon the dose-response model that has been chosen to characterize low dose effects. The following subsections discuss the details of the Committee's analysis.

3.1.2.1 Arsenic Exposures Through Food

The NRC report summarized available information on arsenic in food supplies. These estimates are based on combining information on average diets by sex and age groups with data available on the total arsenic content of the foods included in the diet. The average diets are based on FDA Total Diet Study for Market Baskets Collected for various time periods. For the 1991- 1997 period, total arsenic intake ranged from 2.15 µg/day for 6-11 month infants to 99.1 µg/day for 60-65 year males (NRC, 1999, Table 3-6).

Total arsenic consumed in foods is not directly comparable to total arsenic in drinking water in terms of toxicity. Seafood contributes about 90% of the total arsenic intake from food. Much of the arsenic in seafood is in two organic forms – arsenobetaine (AsB) and arsenocholine (AsC). These two forms are considered nontoxic, although, their carcinogenic potential has not been fully evaluated. In contrast, drinking water primarily contains inorganic arsenate and arsenite, both of which are considered toxic.

For comparisons between arsenic in food and arsenic in drinking water, estimates of the inorganic arsenic in food have been made by assuming that 10% of the total arsenic in seafood is inorganic and that 100% of the total arsenic in food of terrestrial origin is inorganic. For adults, the average inorganic arsenic intake from foods, based on the above percentages, is 10 µg/day (NRC, 1999, p. 47). Average inorganic arsenic intake from food ranged from 1.34 µg/day for 6-11 month old infants to 12.54 µg/day for 60-65 year old males (NRC, 1999, Table 3-6).

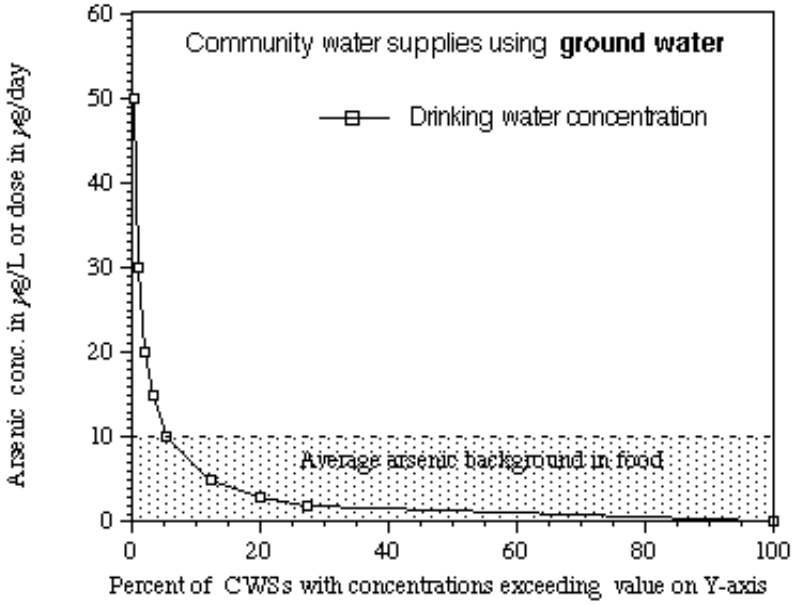
EPA cites the work of MacIntosh, et al. (1997) for an indication of individual variability in inorganic arsenic intake from food. MacIntosh studied 785 adults and found a mean inorganic arsenic intake of 10.22 µg/day, with a standard deviation of 6.54 µg/day and a range of 0.36-123.84 µg/day, using semi-quantitative food surveys. This variability is apparently due to variations in diet rather than variations in the inorganic arsenic content of individual foods.

Neither the NRC (1999) nor the EPA (2000) notes any information on regional variability in arsenic content in foods within the United States. Generally speaking, the food supply within the United States is considered to be rather homogeneous (Schoof et al., 1999). This is not to suggest that some individuals do not have substantial differences in their arsenic intake via food.

3.1.2.2 Arsenic Concentrations in Drinking Water

Using compliance monitoring data from 25 states, the EPA estimated the numbers of ground water and surface water Community Water Systems (CWS) with treated water falling in various ranges of arsenic concentrations (EPA, 2000, Table V- 3 and V-4). Using this information, the Committee prepared concentration exceedency curves for CWSs using ground and surface waters (Figure 1). The EPA tables provided information whereby percentages of CWSs having concentrations exceeding 2.0, 3.0, 5.0, 10.0, 15.0, 20.0, 30.0 and 50.0 µg/L could be determined. These concentrations represent the points plotted in Figure 1. EPA states that the distribution of arsenic concentrations in CWSs is independent of the size of the CWS (EPA, 2000). Consequently the plots of concentration exceedency curves for CWSs also represent concentration exceedency curves for the entire population served by ground water and surface water CWSs. It is evident from the curves that groundwater has much higher arsenic concentrations than surface water. It is also evident from the curves that, while most CWSs

have concentrations below the proposed MCL, treated water from some CWSs has arsenic concentrations considerably in excess of the proposed MCL.



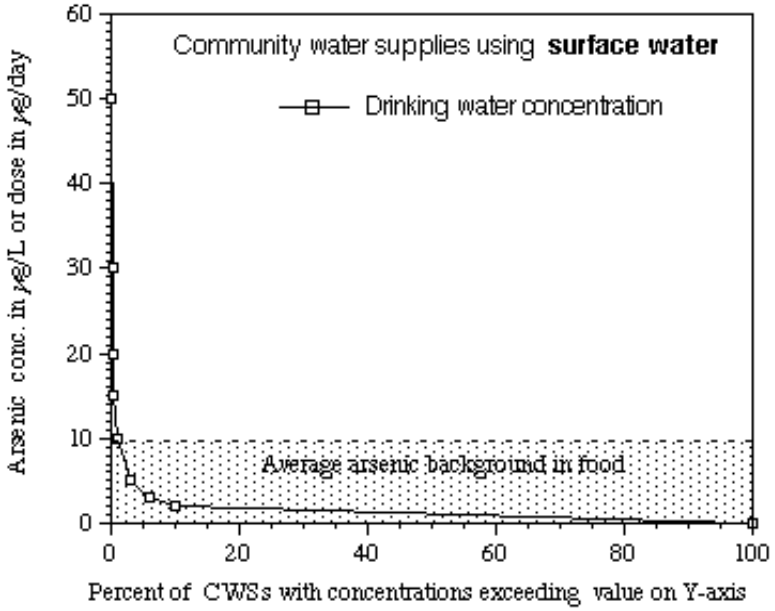


Figure 1. Arsenic concentration exceedency curves for community water supplies using ground and surface waters in relation to average arsenic intake in food. Community water supply data from tables V-3 and V-4 in the EPA proposed arsenic rule. (see text for explanation)

The above data can be used to estimate the population-weighted average concentrations of arsenic in drinking waters from ground and surface water CWSs. For this estimate, the percentage of the CWSs in each interval (e.g. >10.0 to 15.0 μg/L) was multiplied by the midpoint concentration for that interval (e.g. 12.5 μg/L) to obtain a weighted concentration for that interval. Summing the weighted concentrations for all intervals gives the average concentration. For ground water supplies the average concentration of arsenic is 2.85 μg/L,
while for surface water supplies the average is 1.46 μg/L. Since surface water serves 66% of the total population on CWSs and ground water serves 34%, the overall weighted average concentration of arsenic in drinking water is 1.93 μg/L.

3.1.2.3 Comparison of Arsenic Intake from Food and Drinking Water

Figure 1 also represents the relative intake of arsenic from food and water. EPA notes that the average consumption of drinking water from CWSs is 1.0 L/day (EPA, 2000). The drinking water consumption rate of 2 liters/day for an adult, which is often used to estimate doses for drinking water, actually approximates the 90th percentile intake (EPA, 2000). Because the arsenic intake in food is the average dietary intake, the Committee decided to calculate drinking water intake based on average drinking water consumption, rather than the 2 L/day consumption used by NRC (1999).

With an average drinking water consumption of 1.0 L/day, the Y-axis in Figure 1 represents both the concentration in μg/L and the dose in μg/day. The food intake is represented by the gray area on the graph under the dashed line at 10 μg/day. Comparisons of the area under the drinking water exceedency curve with the area of the food "curve" reflect the relative contributions of each pathway to the total intake of inorganic arsenic in the diet.

The relative contributions of drinking water and food to total arsenic intake at the current MCL of 50 μg/L are shown in Table 1. Data are included for ground water and surface water supplies, as well as for the weighted total for the entire population of CWSs (both ground and surface). On average, drinking water contributes 16.3% of the inorganic arsenic intake and food contributes 83.7 %. Thus, water treatment to reduce drinking water concentrations has limited potential to reduce total arsenic intake. However, for the part of the population consuming drinking water with high arsenic

concentrations, water treatment can result in substantial reductions in combined food and water intake. For individuals consuming water at 50 µg/day, arsenic intake in water is five-fold higher than average food intake.

Table 1. Average contributions of drinking water and food to total arsenic doses for ground water CWSs, surface water CWSs, and weighted average for all CWSs.

Water Source	Pathway	Average Arsenic dose (mg/day)	Percent by Pathway
Ground Water (GW)	Water	2.85	22.2
	Food	10.0	77.8
	Total	12.85	100
Surface Water (SW)	Water	1.46	12.7
	Food	10.0	87.3
	Total	11.46	100
Weighted Average	Water	1.93	16.3
(0.34 GW and 0.66 SW)	Food	10.0	83.7
	Total	11.93	100.0

3.1.2.4 Effects of MCL Choice on Drinking Water and Total Intake of Inorganic Arsenic

The DWC used the EPA data from which Figure 1 was produced to calculate the reductions in drinking water concentrations and total arsenic intake that would accompany various choices for the MCL. Those data, along with ancillary data, are shown in Table 2 and Figures 2 & 3. The effects of treatment to reduce drinking water concentrations can be viewed as truncating the portion of the area under the drinking water exceedency curve (Figure 1) at the level of the MCL. The reduction in the

area under the curve reflects the effect of treatment on average drinking water concentrations. For these calculations, we assumed that the arsenic concentrations for all supplies having higher concentrations than the proposed MCL would be reduced to 80% of the MCL value. This is the same assumption as that made by the EPA (2000). The effects of MCL choice on average drinking water concentrations are shown in Figure 2. Imposing an MCL of 5.0 μg/L would reduce the average drinking water concentrations from its current value of 1.93 μg/L to 1.40 μg/L.

The reductions in peak concentrations and the percentage reductions in peak concentrations associated with each proposed MCL are also shown in Table 2. It should be noted that reductions of these sizes would only occur for individuals consuming water at or near the current 50 μg/L MCL value.

Table 2. Effects of arsenic MCL selection on average concentrations in drinking water, on percent reductions in average arsenic doses in drinking water and in food plus drinking water, on the reductions and percent reductions in peak concentrations, and on the number of CWSs requiring treatment to reach the MCL.

Parameter	Current MCL (μg/L)	Proposed MCLs			
	50 μg/L	20 μg/L	10 μg/L	5 μg/L	3 μg/L
Average Ground Water Concentration (μg/L)	2.85	2.52	2.15	1.71	1.39
Average Surface Water Concentration (μg/L)	1.46	1.38	1.34	1.24	1.14
Weighted Average DW Concentration (μg/L)	1.93	1.77	1.62	1.40	1.23
Percent Reduction in DW Concentration/Dose	0	8.3	16.3	27.7	36.5
Percent Reduction in DW Plus Food Total Dose	0	1.3	2.6	4.5	5.9
Reduction in DW Peak Concentration (μg/L)	0	30	40	45	48
Percent reduction in DW peak concentration	0	60	80	90	94
Number of CWSs Requiring Treatment	0	929	2,455	5,621	9,330

The percent reductions in drinking water doses and total doses (DW + food) for various MCL choices are shown in Figure 3A and Table 2. At an MCL of 20 µg/L, drinking water and total doses are reduced by 8.3% and 1.3% respectively, while at an MCL of 3 µg/L, they are reduced by 36.5% and 5.9%. Because drinking water currently comprises only 16.3% of the total inorganic arsenic intake, and most of the population already consumes drinking water with arsenic concentrations less than 3.0 µg/L, the potential for reducing total arsenic intake is only 5.9% at the lowest MCL we are to consider.

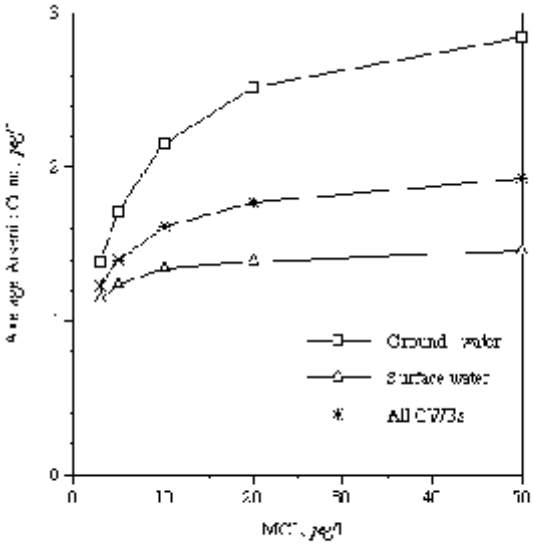


Figure 3. Effects of MCL level on average arsenic concentrations in ground water CWSs, surface water CWSs and weighted average drinking water from all CWSs.

The number of treatment plants required to achieve the reductions in arsenic intake associated with MCL choices is shown in Figure 3B. The slopes of these curves represent the efficiency (reduction/CWSs requiring treatment) of reducing arsenic exposure associated with various MCLs. The efficiency in reducing exposure for going from an MCL of 50 µg/L to 20 µg/L is 3.5 times greater than the efficiency in going from 5 µg/L to 3 µg/L.

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2
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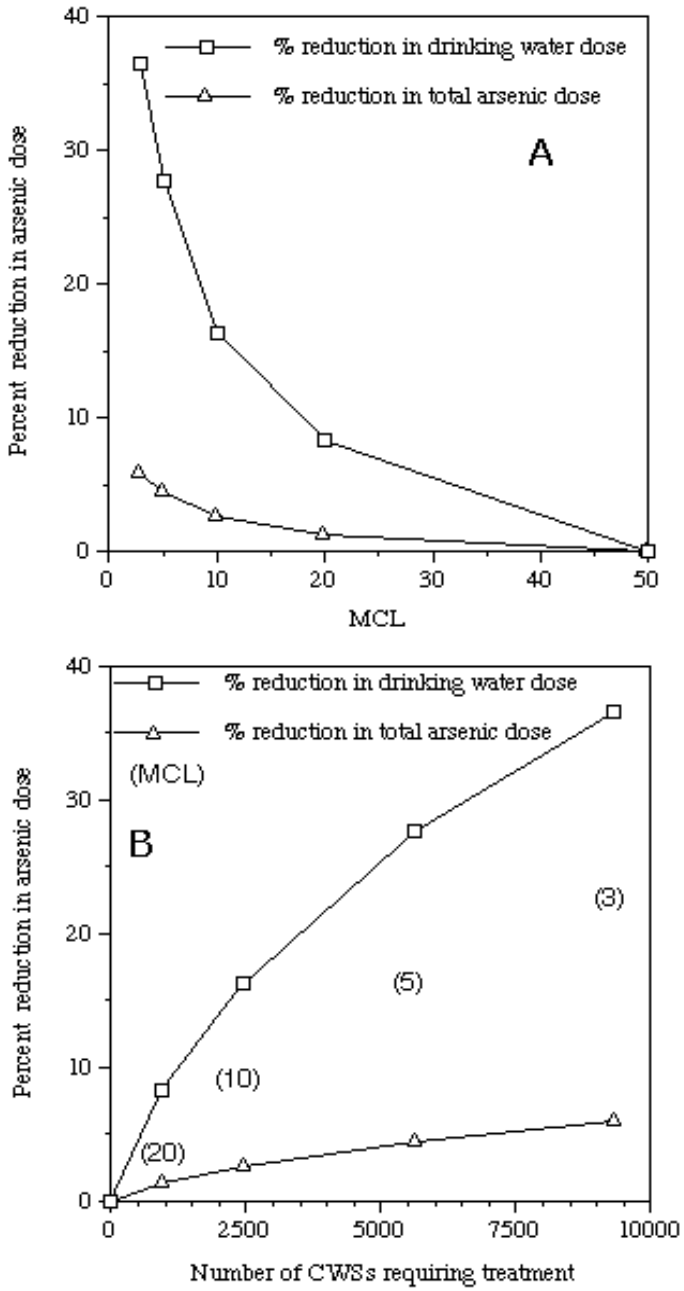


Figure 3. Relationship between percent reduction in drinking water and in total arsenic dose and choice of MCL (A) and number of CWSs requiring treatment (B).

3.1.2.5. Effects of MCL Choice on Health Benefits

The relative contribution of these two sources to health effects at different MCL choices, depends on the choice of the dose-response curve used to describe risk of arsenic health effects at low doses. The EPA has used linear extrapolation of the effects of arsenic intake on bladder cancer for calculating health benefits. However, the mechanisms potentially responsible for arsenic induced cancer were cited by the NRC (1999) as being non-linear.

i) Linear dose-response curve

If the dose response curve is linear, then the health benefits are directly proportional to average doses. The changes in health benefits associated with changes in MCL are directly proportional to the changes in drinking water and total doses presented in Table 2 and Figure 3. At an MCL of 3.0 μg/L, the adverse health effects associated with drinking water arsenic would be reduced by 36.5% while adverse health effects associated with total arsenic intake (food + water) would be reduced by 5.9%. Other MCL choices are accompanied by smaller reductions in adverse effects.

As discussed earlier, we do not really know what the equivalency of the various forms of arsenic are in their intrinsic contribution to the development of cancer in the Taiwanese population. Given that the Agency has chosen linear extrapolation, the DWC recommends that the Agency simply look at the incremental risk associated with drinking water, as that is the controllable risk. Nevertheless, progressing to ever lower arsenic levels, below those levels found in the U.S. diet, is an effort in ever diminishing return in mean arsenic exposure per dollar invested in water treatment.

ii) Sublinear dose response curve

If the dose-response curve is sublinear, reductions in exposure in the high ranges of exposure would have larger health benefits, and reductions in exposure in the low range of exposures would have smaller health benefits, than their corresponding reductions in average concentrations. Under a linear dose-response curve, an MCL of 3 μg/L reduced adverse health effects by a factor of almost 4.5 times that achieved by an MCL of 20 μg/L (reduction in average concentrations by 5.9% and 1.3% respectively). Under a sublinear dose-response curve, the ratio of the health benefits at an MCL of 3.0 μg/L to that for an MCL of 20 μg/L would be less than 4.5 fold, possibly much less. Under a sublinear dose-response curve, the curves in Figure 3B would shift such that the slope (efficiency) between MCLs of 50 μg/L and 20 μg/L would be relatively steeper and the slope between 5 μg/L and 3 μg/L would be relatively flatter.

Under a sublinear dose-response curve there will be a region where exposures to arsenic from food and drinking water begin to interact significantly. The benefits of water treatment depend on where the reductions in total dose (food + water) occur along the dose-response curve. This would require a well-defined sublinear dose-response curve. The generation of such a curve would require an improved understanding of the mechanisms by which arsenic induces its adverse health effects. Generation of a Sublinear dose-response curve from current epidemiological studies would likely be very difficult due to the general lack of measurable health effects in the low dose range.

iii) Threshold dose-response curve

If the dose-response curve includes a threshold value then the arsenic doses from food and water will interact. If the total dose exceedency curve spans the threshold value, only that portion of the exceedency curve above the threshold is accompanied by adverse health effects. The procedures for estimating the health benefits of various MCL choices would be similar to those listed above for a sublinear dose-response curve. Information on the shape of the dose-response curve in the portion of the curve above the threshold value would be needed as well as the threshold.

3.1.2.6 Discussion

In attempting to reduce the frequency of bladder cancers by reducing drinking water exposure to arsenic, the EPA is working in an area where the marginal risk reduction is small. For example, there are approximately 53,000 new cases of bladder cancer each year with 12,000 bladder cancer fatalities. The number of bladder cancers attributable to arsenic can be estimated under the assumption of a linear response of bladder cancers to total inorganic arsenic dose. At an MCL of 3.0 µg/L, EPA estimated an annual reduction in bladder cancers of 22-42 cases and a reduction in fatal bladder cancers of 5.7 to 10.9 per year (EPA, 2000). At an MCL of 3.0 µg/L, the total dose of arsenic is reduced by 5.9%. If a 5.9% reduction in arsenic dose results in a 22-42 case reduction in bladder cancer occurrence, then a 100% reduction would result in a 373 to 745 case reduction under a linear dose response relationship. Under this reasoning arsenic would be responsible for 0.7% to 1.4% of all bladder cancers in the United States. At an MCL of 3.0 µg/L, the accompanying 5.9 % reduction in total arsenic dose would reduce bladder cancers in the United States by 0.04% to 0.08%. At the proposed MCL of 5.0 µg/L, EPA states that there would be 16 to 36 fewer occurrences of bladder cancer. These represent reductions 0.03% to 0.07% in the annual occurrence of bladder cancers in the United States. Smoking and occupational exposures are thought to be the major causes of bladder cancer.

3.1.2.7. Recommendations

The above analyses indicate that average arsenic ingestion via food is considerably larger than average arsenic ingestion via drinking water even at the current MCL of 50 µg/L . For the limited

populations where drinking water concentrations are at or near the current MCL, considerable reductions in total arsenic exposure can be achieved by reducing the MCL. By assuming a linear dose-response curve, the EPA was able to calculate the marginal benefits of drinking water treatment, even though food represents the major pathway of arsenic intake. If the mode of action supported a nonlinear response to total inorganic arsenic intake, food and water pathways would both have to be considered in calculating treatment benefits. Such calculations would require a well-defined nonlinear dose-response curve and more information on the distribution of food intakes, neither of which are currently available. Consequently, the DWC concurs that EPA had no choice other than to proceed with marginal risk reduction calculations based solely on considerations of drinking water risk reduction as calculated using a linear response model and ignoring food intake. However, it is also clear from the above analyses that there is a limit in the benefits that can be realized by reducing arsenic in drinking water. It should be kept in mind that regardless of the MCL chosen between 5 and 20 μg/L only the extreme levels will be reduced in drinking water. Conversely, the extremes in arsenic content of foods will remain unaltered by this regulatory action.

3.1.3 Charge Question 3: Health Advisory on Low Arsenic Water and Infant Formula

Formula. The NRC report was inconclusive about the health risks to the pregnant woman, developing fetus, infants, lactating women, and children. Given the potential for cardiovascular disease (as evidenced by EPA's Utah studies and extensive other data) and uncertainty about risks to infants, EPA plans to issue a health advisory to recommend use of low-arsenic water in preparation of infant formula. Is this precautionary advice appropriate given the available information?

EPA plans to issue a health advisory to recommend use of low-arsenic water in the preparation of infant formula. This advisory would be active during the period covering the interval between promulgation of the final rule and its full implementation, a period from 3 to 5 years. The DWC held extensive deliberations on the implications of such a health advisory. During the discussion, EPA provided more detail about the type of health advisory envisioned and how it would be disseminated. The advisory would note that the exposure standard has been lowered but that implementation will be delayed for a period of years and in the interim parents concerned about arsenic risk to infants should consider using low arsenic water to prepare infant formula. The action contemplated by the EPA is different from the health advisories issued in the past and with which many of the DWC members are familiar. This was a source of confusion in the discussion, in particular it was not understood initially that this was an interim measure, rather than a lower exposure recommendation for infants. The intent of the advisory is to alert parents that they may want to take actions to protect their children against this potential risk in the period before the standard comes into effect.

The motivation for issuing an advisory is concern about health risks to the developing child and uncertainty about cardiovascular risks to infants (that would be expressed later in life) as well as the higher exposure in infants. It recognizes that children are not young adults. Differences in size, maturity of biochemical and physiological functions in major body systems, and variation in body composition (water, fat, protein and mineral content) all can modulate the severity of toxicity to any toxicant in a rapidly developing fetus-infant-child, including arsenic. Because newborns are the group most different anatomically and physiologically from adults, they can exhibit the most pronounced quantitative differences in sensitivity and susceptibility to environmental toxicants, including arsenic.

The DWC attempted to reach consensus on the need for a health advisory; however, the Committee was not able to agree on the need for such a warning. This was in large part because the Agency was not able to provide sufficient details on the content of such an advisory. Several members expressed concern that the advice sought was on a policy recommendation, rather than the scientific basis for such a recommendation. The DWC did consider policy concerns, including whether such an advisory could be developed to warn and inform without alarming the intended audience, whether a focus solely on infants was appropriate (or whether pregnant women should be warned), and whether alternatives would be available.

As a result, the Drinking Water Committee identified a number of concerns during its discussion which it wishes to pass along to the Agency. These concerns and items that should be considered by EPA if it intends to issue an advisory include:

i) What should be recommended? The DWC was of one mind that it was not the proper entity to design this advisory. However, there were many concerns, voiced by those in favor of an advisory as well as those who opposed it, that this would have to be done very carefully. It is not at all analogous to other health advisories issued by the Office of Water and perhaps should be identified as something other than a health advisory to avoid confusion.

ii) Any health advisory of the type contemplated should focus on health professionals (pediatricians and public health officials) and not be issued broadly to the public. These are the people in the community that can be depended upon to find alternatives within that community.

iii) Alternatives must be identified that are reasonable for the community that is being notified. Bottled water will not have to be in compliance with the new arsenic standard, at least not immediately.

iv) What do we know about the arsenic content of baby foods and prepared formula?

v) The recent data (Hopenhayn-Rich et al., 2000) suggestive of a link between arsenic in drinking water and still birth or neonatal mortality are based on exposure to a very high

concentration of arsenic (860 µg/L). While children must be considered to be at greater risk for a toxic response to any agent in water because they have a greater water consumption when adjusted for body weight, there is no evidence of heightened sensitivity or susceptibility to arsenic demonstrated by this study. The concentrations possibly associated with adverse reproductive outcomes are also associated with toxicity in adults. There are significant uncertainties in the risks for developmental toxicity, cancer and vascular disease at exposures in the 5-50 µg/L range that the advisory would address. The Committee noted that in the Hopenhayn-Rich, et al., study the increases in still birth or neonatal mortality disappeared after the arsenic concentration in the Antofagasta drinking water fell to 110 µg/L or less (Figure 4). At that point, the stillbirth or infant mortality experienced in Antofagasta (that previously had high arsenic water) was similar to that of the control town, Valparaiso, with arsenic concentration around 5 µg/L. Sometimes the exposed town was less than and sometimes greater than the control town; these were small differences, not in a consistent pattern and appeared to be due to randomness in the data (which were averaged over 4 year periods because there was considerable variation from year to year). Other are data indicate children may differ somewhat in the extent of arsenic methylation, however, it is not clear if this would increase or decrease toxicity.

vi) The DWC felt that if an advisory is to be developed it should inform without alarming. Information should be provided that ensures that as a result of an advisory, choices are not made that might subject children to dehydration, inadequate nutrition, or other unanticipated risks as a result of this advisory.

vii) This is a policy issue, not a science issue.

Attachment A to this report, *A Minority Report on Arsenic in Drinking Water: The Unique susceptibility of Children to Arsenic*, by Dr. John Rosen, a consultant to the DWC for the Arsenic Review provides an analysis of issues relative to the differential sensitivity of children to arsenic that departs from the majority opinion contained in this report. Dr. Rosen is joined in this dissenting view by Dr. Barbara Harper, a member of the Drinking Water Committee.

3.2 Comments on EPA's interpretation of the NRC report:

3.2.1 General Comments

This section of the report discusses some uncertainties associated with the Taiwanese study data used to estimate risks to U.S. populations from arsenic in drinking water. The DWC believes that the Agency may have misinterpreted the intent of the statistical analyses of the Taiwanese data and the interpretation of the risk statements that were provided in the NRC (1999) report. The NRC panel was careful to point out that it did not mean to imply that its analyses are formal risk assessments (see

page 264). Rather the panel evaluated different models as a means of exploring the utility of the available data for use in estimating the risk of bladder cancer from arsenic exposure. The DWC learned of a broader set of analyses that have been published since the release of the NRC report.

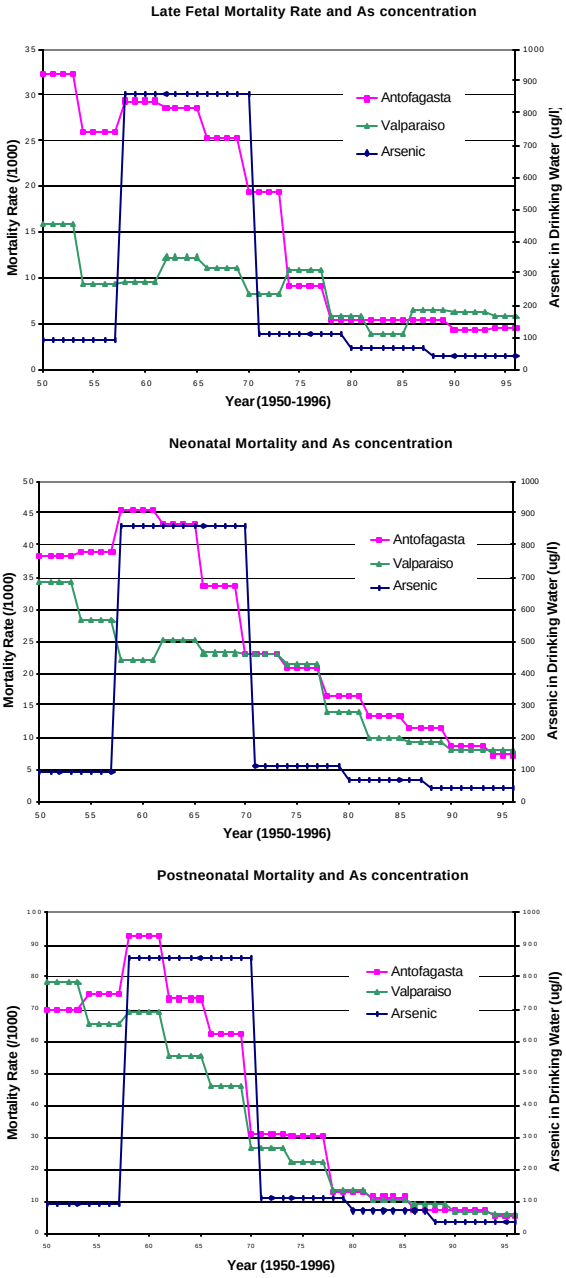


Figure 4. Arsenic Exposure and Reproductive Outcomes.*

*Note: Data are drawn from Tables 2 and 3 in Hopenhayn-Rich, et al. (2000). Because the water concentration and outcomes data were grouped into different time brackets in the two tables, results have been graphed by year. The concentration data are for the

town of Antofagasta. A new drinking water source for Antofagasta was introduced in 1958: this source was high in arsenic and the concentration of arsenic in drinking water increased. In 190, an arsenic-removal plant was installed and the arsenic concentration in the drinking water fell. The control town, Valparaiso, has no historical evidence of high arsenic concentration. The concentration is described in the text below as 5 ug/L in recent surveys and below the detection limit (20 ug/L) in monitoring performed by the water company between 1990 and 1994.

Ordinarily, epidemiology studies compare the disease incidence in an exposed population with a group that has lesser exposure (i.e., a comparison population). However, if there are substantive differences in the characteristics of the comparison population, the differences noted may not be valid. It is possible to model dose-response without a comparison population by simply looking at the response rates within the exposed population as a function of the gradation of exposure. Some unrealistic risk estimates can be derived from the Taiwanese data suggesting that the use of comparison populations (i.e., the whole of Taiwan, or even the remaining portions of southwestern Taiwan) is inappropriate. The utilization of these data also tend to distort the dose-response curves obtained with the linear model. This suggests that there are unique features of the population found in the Taiwan study area. In the following paragraphs, this issue is discussed in some depth based on the DWC's analysis of the report by Morales et al. (2000).

Morales et al. (2000) focused extensively on the impact of including a comparison population in the analysis of the Taiwanese data. As discussed in the NRC report, the available internal cancer data are based on 42 villages from the arsenic endemic region, hence all have non-zero exposures to arsenic. Benchmark doses (BMDs) can be computed from a dose response model fitted to the village data and extrapolated to zero, or from models that use population-based data to specify expected cancer rates at the zero level of exposure. In contrast to the NRC report, which found high concordance between analysis with and without inclusion of a comparison population, the expanded analyses of Morales et al. suggests that estimated BMDs are highly sensitive to inclusion of a comparison population. In addition to data on the whole of Taiwan as was done in the NRC report, Morales et al. also considered a smaller comparison population based only on the southwestern region of Taiwan.

The expanded analyses of Morales et al, which included log and square root transformations of exposure, suggested that BMDs derived from models that included a comparison population could be an order of magnitude lower than those based on models that did not include a comparison population. For example, Morales et al. found that a 1% BMD of 23 μg/L for male bladder cancer from the best fitting model including the whole of Taiwan as a comparison population. The analogous result based on using only the southwestern region was 54 μg/L. In contrast to the variability of BMD estimates based on models that included a comparison population, Morales et al. (2000) found a high degree of stability for models fitted without use of a comparison population: 1% BMD estimates were consistently found to be around 400 μg/L.

Morales et al. (2000) also extended the NRC analysis to consider additional classes of dose response models and by including lung in addition to bladder cancer. An important finding was that arsenic associated risks from lung cancer were of a similar magnitude to those for bladder cancer. For example, the 1% BMD for lung cancer based on the best fitting model (no comparison population) was 343 μg/L for males and 256 μg/L for females.

After some extensive discussion, the DWC was convinced that there are some good reasons to rely on the estimates based on models that do not include a comparison population. For one thing, if the lifetime cancer risk at the current standard (50 μg/L) was really 1 case in 100 persons in the population, or greater, then there should be more evidence of effects in the US. For example, despite some methodological shortcomings, the committee felt that the data available from the Lewis et al. (1999) study in Utah were not consistent with risks greater than 1 in 100. The DWC believes that there are several possible reasons for not using models that include Taiwan-wide data as a comparison population. These include: (1) lifestyle differences between the poor, rural population in the arsenic endemic region and the general population which are likely to alter baseline cancer rates and (2) the likelihood that the population in the arsenic endemic region was also being exposed to additional arsenic in food. This could mean, for example, that someone classified as being exposed to 40 μg/L in water might actually have received a total exposure of 80 μg/L. BMDs calculated from models that include a comparison population will be particularly sensitive to bias in this setting, since the general population will not have the same background levels of arsenic or the same nutritional status as the study population. In contrast, analyses that use only data from the arsenic endemic region should provide fairly accurate estimates of the risk associated with incremental increases in the amount of arsenic in drinking water.

The DWC concluded that issues related to choice and inclusion of a comparison population are also problematic for the Utah study (Lewis, et al., 1999). The study population in Utah was based on records from the Church of Jesus Christ of the Latter Day Saints. Just as in Taiwan, there are good reasons to believe that the analysis could be confounded by lifestyle differences between the study population and the general population in Utah. Indeed, the variability seen in the standardized mortality ratio (SMRs) reported in the study emphasizes this concern. The DWC recommends that additional analyses be performed using data only from the study population and focusing on dose response within that population. The DWC is also concerned about the way in which exposure levels were categorized in the Utah study: by classifying subjects in terms of ppb-years of exposure, the study induces an association between exposure and age. The DWC recommends that the analysis be done with exposure represented by concentration in drinking water, not ppb-years of exposure. Then adjustments for cumulative exposure can be made separately.

With respect to the Utah study, it is important that the Agency complete the analysis of these data. In terms of the cancer risk, this analysis is important for establishing the range of uncertainties that

come from attempting to adapt data from Taiwan to estimating dose-response characteristics for the U.S. Although the data provided in published results of this study imply that there was no excess bladder or lung cancer in this population, the data are not in a form that allows dose-response to be assessed dependably. In the public comment period during the June 5-7, 2000 DWC meeting, the Committee learned that some of these data were being reanalyzed and that some changes in the results could occur. The completion of these analyses are important to the longer term consideration of arsenic risk in drinking water. However, the Committee does not think that the Agency should delay decreases in the MCL while the reanalysis is completed.

In summary, the Morales paper is a useful expansion of the analysis provided in the NRC report. Risk estimates based on the use of population-based comparison groups appear to be unstable and lead to risk estimates that are unrealistically high. There is good reason to rely on the estimates that use only the data from the study area (i.e., no comparison population). These estimates consistently and stably predict a risk of a magnitude of one in one-thousand for both bladder and lung cancer at the current MCL of 50 ug/L.

The remainder of this subsection focuses more specifically on some of the factors that might account for differences in apparent susceptibility of the Taiwanese population to cancer and other adverse health effects relative to the U.S. population.

3.2.1.1 Shortcomings of the Taiwanese data.

As pointed out by NRC (1999), the Taiwan data has serious limitations for use in a quantitative risk assessment. Below, we briefly describe uncertainties that make it impossible to determine the extent to which well known risk factors for lung and bladder cancer might have contributed to the observations in Taiwan and therefore, have implications for arriving at an MCLG. This is not simply a question of inadequate knowledge of the smoking habits, endemic disease and nutritional factors within the population, but of whether these factors might significantly modulate the arsenic effect. Considerable evidence has accumulated in recent years that arsenic has more marked properties as a cofactor (e.g. cocarcinogen, promoter, and perhaps progressor) than as the sole initiator of cancer. The area in Taiwan in which the arsenic exposed population lives is rural, quite poor, and has varying degrees of evidence of nutritional deficiencies that may be reasonable contributors to the observed effect either directly or indirectly enhancing the effects of arsenic. The sensitivity of the risk estimates to the use of comparison groups of the whole of Taiwan, or even the Southwestern area of Taiwan that includes the study population, highlights this issue. Comparing these results to the assessment of risk over gradients of arsenic suggests the possibility that these other factors also contribute to cancer risk in the area. This is because the dose-response curve can be viewed as having a non-zero intercept on the Y-axis when only the study population is considered. There are other possible interpretations, but some of the estimates provided with other comparison groups result in risk estimates of as much as 1 in

100 at concentrations in the 20 µg/L range. Risks this high are hard to reconcile with the observations in U.S. populations, because drinking water levels approach this concentration in many parts of the U.S. and no such results have been observed. Despite its limitations, the results of the Utah study also suggest there are potential differences between the affected population in Taiwan and the U.S.

Considering the above factors leads to a conclusion that transferring the dose response curves describing the cancer risk in this section of Taiwan to the U.S. is likely to bias U.S. risk estimates towards overestimates. The magnitude of this bias could be large, but the DWC does not have the resources to resolve these issues more definitively.

3.2.1.2 Effects of nutrition and preexisting disease in populations that have been studied

A number of mitigating circumstances were identified in the NRC (1999) report that suggest that risk levels calculated from the Taiwan data should not be rigidly extrapolated to the U.S. population. Poor nutritional status is known to be characteristic of this population and others (Chile, India) that have been studied. A recent cohort study in Utah (Lewis et al., 1999), found no evidence of either bladder or lung cancer where mean drinking water concentrations of arsenic approached 200 µg/L. While these concentrations are up to an order of magnitude lower than found in sites where positive associations with cancer have been obtained, these results give rise to significant questions about whether the Taiwan data apply quantitatively to those U.S. populations that have a more adequate nutritional status.

Experimental work in animals establishes that deficiencies in selenium substantially increase the toxicity of arsenic (Pan et al., 1996; Oster, 1992). The NRC (1989) report summarizes the results from a survey of urinary selenium concentrations in Taiwan and other parts of the world. Essentially, the study population in Taiwan was estimated to have selenium intakes that were only 25% of the recommended dietary intake (NRC, 1989). Their intakes are less than 50% of the safe range identified by the World Health Organization (WHO, 1996). For this reason NRC recommended that the selenium status of the Taiwan population be taken into account in transferring the data to populations that are selenium sufficient. Neither NRC or EPA made an attempt to make these adjustments. With a limited search, the DWC identified a number of studies that have documented substantial effects of smaller selenium decrements on cancer of the bladder (Helzlsouer et al., 1989) and lung (Salonen et al., 1985; van den Brandt et al., 1993). The DWC strongly recommends that the Office of Water take this factor into account when arriving at an MCL. The Committee expects that additional data exists that could be used for estimating the extent to which nutritional deficiencies of the magnitude identified in Taiwan have on arsenic toxicity in general and on carcinogenicity specifically.

The other nutritional issue that has been identified in the Taiwanese population from which the data were obtained, was the potential for less than optimal intakes of methyl donors in the diet, such as methionine or choline. There are data to suggest that hypomethylation (as well as hypermethylation) of DNA does occur with exposure to various forms of arsenic (Zhao et al., 1997 as quoted by NRC, 1999). Choline deficiency has long been used experimentally as a tumor-promoting regime in animals (Lombardi et al, 1994; Saito et al., 1994), therefore it is probable that substantive deficiencies in the diet could increase sensitivity to arsenic induced cancer in humans. However, the NRC committee did not indicate whether such deficiencies were documented in the Taiwanese population studied. There were indirect indications of what made up a substantial portion of the diet (rice and sweet potatoes), but the estimates were not quantitative, nor were other constituents of the diet discussed in quantitative terms.

Other characteristics of the Taiwanese diet may also have contributed to the increased susceptibility to cancer. Zinc insufficiency is also present in the blackfoot region of Taiwan. Zinc can protect against acute arsenic toxicity, although its influence on the chronic effects of arsenic are not known. For the study population the diet consisted of 9% protein, while fat contributed 5% of the caloric intake. Poor diets may have also involved limiting levels of folate, methionine, cysteine, and B12.

In some Asian countries endemic infectious hepatitis has been known to be important in sensitizing populations to the hepatocarcinogenic effects of aflatoxin (Caselman, 1996). It would be useful to consider the incidence of infectious hepatitis in the study area of Taiwan to determine if that might contribute to the increased risk for liver cancer found in some studies. The NRC did not consider this recognized risk factor in its deliberations. The DWC suggests that EPA attempt to find out whether the area studied in Taiwan also has high rates of hepatitis which is known to act as a co-carcinogenic factor in liver cancer.

In summary, the characteristics of the Taiwanese population studied for arsenic carcinogenesis are not typical of the characteristics of the general U.S. populations, but there may be segments of the U.S. population which have one or more of the same potential co-risk factors as the Taiwanese population. The prevalence of the risk factors mentioned above need to be evaluated in both the Taiwanese and U.S. populations. These differences raise significant uncertainties about the accuracy of risk estimates that are based on the Taiwanese data. Unfortunately, the DWC cannot be more quantitative in its own assessment for lack of resources and time. For this reason, we join with the NRC (1999) recommendation that the Agency develop a more formal risk assessment that attempts to take these factors into account. However, this should not significantly delay promulgation of a rule that makes a significant reduction in the MCL for arsenic as there may be populations with similar nutritional deficiencies within the U.S.

3.2.1.3 Modes of action attributed to arsenic are sublinear.

Cancer has been produced in experimental animals with arsenic, but a measurable response has been most readily observed when combined with other treatments, such as the use of a tumor initiator (see Shirachi et al., 1983; Laib and Moritz, 1989). Yamamoto et al. (1995) using several different initiators, found DMA to be an effective promoter in the lung, bladder, kidney, liver and thyroid gland of the rat. The site concurrence for these tumors with the human data should be of interest. Wei et al. (1999) and Arnold et al. (1999) demonstrated that high doses of dimethylarsinic acid can produce bladder carcinogenesis in the rat and Ng et al. (1999) found that tumors of the lung, gastrointestinal tract, and liver were produced with 0.5 mg As/kg water as sodium arsenate.

Studies of arsenic's effects at the cellular and molecular level support a sublinear dose-response model (NRC, 1999). Its apparently non-linear effects in producing structural and numerical chromosomal abnormalities through apparently indirect mechanisms are one example. Similar arguments would be developed for the "comutagenic" activity of arsenic. Other plausible modes of action include modification of DNA methylation (presumably caused, in part, by arsenic's competition for methyl donors) are associated with altered gene expression. It would be anticipated that these effects behave in a sublinear way at low doses (i.e. possess effective thresholds).

There are abundant data that associates various forms of arsenic with a variety of mechanisms or modes of action. If they could be shown to uniquely or collectively account for human tumors, the dose-response curve could be viewed as being sublinear at low doses. NRC (1999) pointed out that none of these alternative modes of action have been clearly demonstrated as essential in the development of arsenic-induced tumors. In most cases, even dose-response information showing parallels between those that produce tumors and those that activate these other mechanisms have not been explored. Therefore, the NRC concluded that the prudent course would be to use linear extrapolation. However, the data derived from studies attempting to identify mechanisms that are outlined in much more detail in the NRC report, suggest that applying linear models for low dose extrapolation is not only conservative, but contrary to the data in those reports. In reassessing risks from arsenic in drinking water, the Committee suggests that the Agency explore non-linear models, such as the Moolgavkar, Venzon, Knudson (MVK)

3.2.1.4 Use of experimental data that was available and the need for further research

Considering that the Agency is presumed to be acting under a new set of cancer risk assessment guidelines, the DWC was somewhat surprised that the Agency did not at least provide some summary of the data that are available and how they inform the current risk assessment decision made by the Agency. There have been substantial breakthroughs in the development of animal models

of arsenic carcinogenesis in the past several years. In part these data point up the weakness of some of the arguments that have been made to attribute cancer risk to inorganic arsenic. The relative ease of producing bladder cancers in rats with dimethylarsenous acid requires some shift in the paradigm that was not evident in either the EPA or NRC documents. It is possible that these data are still too limited to be of any use in arriving at risk estimates at this time (NRC, 1999). Moreover, the DWC recognizes that in the case of arsenic where the margins between actual exposures and effects are small compared to most other contaminants, that the final decisions will involve many non-scientific issues. However, these data are essential for identifying susceptible populations and need to be forcefully pursued before the arsenic MCL undergoes another iteration. The fact that they are not acknowledged in the documentation put forward by EPA provides no further encouragement to pursue these issues in the future. Consequently, we have taken this opportunity to comment on some of the research results that the DWC feels provide direction for future research in characterizing the risks of arsenic in drinking water.

Arsenic is not a classical direct acting carcinogen. It does not cause DNA adducts, nor does it induce point mutations although it can replace some of the phosphates in the sugar-phosphate backbone of DNA (Dixon, 1997). This can result in the cleavage of the sugar-phosphate/sugar-arsenate backbone and potentially in single strand breaks. This mode of action might account for the occurrence of deletions and translocations in the absence of point mutations in arsenic-induced cancer. Patrick (1964) demonstrated the incorporation of arsenic into DNA, protein, and lipid at the same rate as PO_4. Furthermore competition between these two ions has been said to uncouple oxidative phosphorylation (Frost et al., 1968). Although this data is weak, it provides a mode of action not yet fully explored.

AsIII can interact with thiols. This type of interaction may be important in the interaction with lecithin cholesterolacyl transferase (Jauhiainen et al., 1988) of potential relevance to vascular changes indicative of atherosclerosis.

Interactions with thiols are significantly involved in the metabolism of arsenic. In serum, arsenic is transported bound to sulfhydryl groups of proteins, GSH, and cysteine. AsIII can form a complex with GSH (Delnomdedieu et al., 1994) and is more generally reactive with tissue than AsV. Moreover, arsenite (not ionized at physiological pH) can be taken up by liver cells and methylated, but not arsenate (ionized at physiological pH). In the kidney, however, arsenate is taken up, reduced, methylated, and released into the urine. The reduction of AsV can be accomplished by sulfhydryls. For example, glutathione can provide a reducing equivalent for AsV and the resulting AsIII can then oxidatively add a methyl through SAM (S adenosylmethionine) to produce the methylarsenic V.

These are only a few animal studies performed in the absence of a co-carcinogen that demonstrate induction of neoplasms by arsenic or one of its metabolites. The induction of bladder

cancer in rats by DMA as reported by Wei et al. (1999) and Arnold et al. (1999) are of particular interest, since bladder cancer is one of the principal sites of concern in humans. These studies must be followed up. Arnold et al. (1999) have indicated that a non-linear mode of action is appropriate for DMA in the rat and hence for cacodylic acid (DMA) in the human. Genotoxic effects of arsenic appear to require substantially higher concentrations of DMA that would be observed systemically in animals provided DMA, since Moore et al., (1997) found concentrations of 5 mg/ml necessary to obtain a positive result in the MOLY assay. The finding of tumors in several organs of mice that have counterparts in the human epidemiology studies, but not bladder, given a relatively low level of arsenate by Ng et al. (1999) are also of interest. With these animal models there is now a much more reasonable path to pursue the mode(s) of action of arsenic and PB-PK analyses that may be responsible for these tumors.

The level of various arsenic metabolites in the urine, the serum, and in the target tissues and cells should be determined in these newly developed animal models. The most important questions are the concentrations and forms of arsenic responsible for each of the tumor types identified in human studies. When that information is obtained, truly useful pharmacokinetic models can be developed that will be very important in identifying the concentrations and species of arsenic formed in humans that are associated with carcinogenesis. This would help to determine the level of inorganic arsenic intake required to obtain the effective levels of arsenic metabolites under different conditions of human exposure. This will provide a much more comprehensive basis on which to determine the relative importance of drinking water and food sources of arsenic.

There are also genetic factors that increase the susceptibility to bladder cancer that might contribute to the background rate of tumor incidence that is independent of arsenic exposure. The prevalence of the GST-mu null and certain polymorphic forms of NAT2* (Bell et al., 1993; Eaton and Bammler, 1999) in the Taiwanese population (Chiou, et al., 1997) were not discussed by the NRC (1999) and, we presume they were not explored. These variables have been important modifiers of risks in smoking populations (Wen, et al., 1994; Salagovic et al., 1999).

4. TREATMENT TECHNOLOGY ISSUES

4.1 Comments on Treatment Technology Issues

4.1.1 Charge Question 4: Disposal Options. Based upon a review of the attached materials, does the SAB believe that the EPA produced an accurate projection of the likely disposal options for arsenic residuals and the distribution of these options by treatment type? What are the SAB's views on the advantages and the limitations of the various waste disposal options? What effect, if any, would the SAB's analysis of these advantages and limitations have on the probabilities assigned? What are the SAB's views on which options will be more likely used by small systems (less than 10,000 people), and which will be more likely used by larger ones?

The committee agrees that EPA has covered the spectrum of residual disposal alternatives. However, the committee feels that certain alternatives are not viable due to potential constraints placed on utilities. It is the consensus of the committee that disposal of ion exchange (IX) or activated alumina (AA) treatment residuals to a publically owned treatment work (POTW) will not be acceptable in the vast majority of systems because of the high Total Dissolved Solids (TDS) concentration in those residuals. This is especially true in the southwest where treated wastewater is reused for irrigation and groundwater recharge and salt concentration is very important. Additionally, POTWs generally are opposed to receiving organically dilute wastes that will reduce the efficiency of biological treatment. This is the case in systems such as in Des Moines, Iowa. This would reduce the probability of selection for those alternatives which rely on these disposal options to near zero.

Additionally, the committee feels that the assumed non-hazardous classification of the waste brines and sludges is not appropriate for the economic analysis. It is clear that in California the wastes would be classified as hazardous and this could result in a public water supply choosing another alternative. Furthermore, the committee has concerns related to the Toxicity Characteristic Leaching Procedure (TCLP) test which is used as the standard test for hazardous waste determination. The TCLP is designed to maintain a pH of 5-6, which represents the best cast scenario for arsenic binding to sludge. Therefore, while an arsenic-laden sludge may pass the TCLP test it may still leach arsenic into the groundwater under normal pH conditions found in some landfills. Additionally, characterization of lime softening (LS) sludge by the TCLP test is suspect because the target pH of the test (pH = 5) is likely to be overwhelmed by the acid neutralizing capacity of LS sludge.

4.1.2 Charge Question 5: Decision Tree for Treatment Technologies. Does the SAB agree with the principal "branches" of EPA's decision tree described in the attached

documents and the likelihood that these options will be used for systems of various sizes with various source water characteristics? What views does the SAB have on EPA's description of the advantages and limitations of these treatment technologies? Would the SAB's views on the these advantages and limitations affect the probabilities assigned?

It was very difficult for the committee to address this charge without having the detailed documentation on the decision tree that was used by EPA to predict technology selection and cost. As a result the committee was not able to follow, nor comment extensively upon, the "decision tree." Generally, the committee feels the cost estimates predicted for the rule appear to be low. From the limited information provided and from presentations to the committee at the June 5-7, 2000 DWC meeting, the model seems to have certain deterministic and probabilistic components that make it quite complex.

In spite of the limitations noted above, the committee does provide the following observations on some of the assumptions used in the model:

i) The list of best available technologies (BATs) seems to overstate the real situation. It is the opinion of the committee that none of the technologies listed as BAT have been demonstrated in full-scale operation for arsenic removal. While it is true that some of the technologies are used in full-scale water treatment, they have not been operated optimally for arsenic removal. This optimization may result in a substantially different control strategy from the traditional operation.

ii) The committee is concerned that the list of BAT technologies may bias technology selection by community water systems (CWSs), and particularly to bias selection against some of the more promising emerging technologies [e.g., granular ferric hydroxide (GFH)].

iii) The model does not appear to account for land acquisition cost. For groundwater systems using multiple entry points, this may be a substantial cost when wells are located on small lots of land within developed portions of a city.

iv) It appears that the cost of replacement chemicals is not included in the cost of removing arsenic. In particular the cost of fluoride replacement when the resulting concentration is below optimum should be included in the cost of arsenic removal.

v) It is not clear that the monitoring burden and costs associated with POU and/or POE systems is adequately represented in the costs for these technologies.

vi) It is not clear that EPA has considered the need for increased training and certification of

operators (or even availability of personnel) for a large number of very small systems. The committee is concerned that this might lead to closure of some of these systems and increased reliance on private wells.

vii) It is clear to the committee that there are uncertainties contained in the model that result in uncertainties in the output. It would be more appropriate to present the output with a range of results than a discrete number. It is the feeling of the committee that the range of uncertainty is larger for an MCL of 5 µg/L as compared to a value of 10 µg/L or 20 µg/L.

4.2 Other Issues Related to Cost Evaluation

4.2.1 Affordability Criterion

The DWC has previously commented on affordability issues (SAB, 1998). In that advisory the DWC called attention to the fact that there was no Agency definition of "national affordability." The Committee anticipated difficulties in utilizing a national criterion in a rule that disproportionately impacts small systems, as does the arsenic rule. Many small communities fall substantially below the national median income. As a consequence the DWC feels that it is questionable that the "affordable" amount derived from the national median income appropriately reflects reality in the impacted communities.

The draft proposed rule states (p. 136) that a median U.S. household can afford 2.5% of its income for water costs. This amounts to an "affordability threshold" of $750/yr. The rule then goes on to state that the median water bill for small systems was about $250/yr, and therefore, there is an available expenditure margin of up to $500/yr. It is also stated that the cost/household of arsenic treatment technologies is below the available expenditure margin of $500/yr, and therefore, no variance technology for any system size has to be identified. In other words, the cost of an arsenic MCL of 5 µg/L is affordable. It is important to remember that in using the median household income that 50% of the population is below this level and the percentage of household income represented by $750.00/yr will be greater than 2.5%.

In this argument, EPA seems to ignore the fact that there are many other regulations that have been promulgated or proposed (e.g., Microbial/Disinfection Byproduct Rule, Groundwater Rule, Long-Term Enhanced Surface Water Treatment Rule, Filter Backwash Rule, etc.), or will be proposed in the near future. If an affordability criterion is to be developed and argued for this rule, a determination has to be made as to the fraction of the available expenditure margin that should be allocated to compliance with a lower arsenic MCL. This fraction has to be somehow related to the risk reduction benefit associated with the lower MCL relative to that associated with other regulatory requirements.

The Agency should consider the multiple tradeoffs that are faced in the situation that exists in

the U.S. population where some small systems and some sensitive subpopulations might co-occur. This situation raises questions about justifying different levels of protection to different populations because of cost and affordability concerns., an environmental justice issue.

If these concerns lead to a suggestion that the systems serving such populations should be allowed to have higher arsenic levels than those serving more economically advantaged populations then one must be concerned with issues of environmental justice–or in this case the situation in which disadvantaged populations are asked to accept higher risks than more advantaged populations because of affordability concerns.

The situation is more complex than just affordability. For example, it is possible that these same households might, as a consequence of nutritional or other factors resulting from their economic situation or because of an increased susceptibility, sustain a greater risk from elevated arsenic levels. In this case, it would be reasonable to expect that the result of any disproportionate cost they would sustain because of a low arsenic MCL would be increased benefits because their gain from risk reduction efforts would be greater than others who were not especially susceptible because of these factors. In that case, the increased cost might be balanced by the increased benefit and be better justified. However, since this is a situation in which some of the increased risk might be attributed to poor nutrition, one might also need to consider whether the allocation of resources to achieve a lower MCL might gain you less than allocating those resources to improved nutrition. Further, economically disadvantaged or susceptible populations do not only exist in areas served by small systems. Many such persons also live in areas served by large CWSs.

The bottom line is that households will pay the cost of arsenic removal. There is no proposal for governmental programs that would take on these costs in lieu of those households. If too high a treatment cost shifts those populations away from a small CWS with some level of treatment, to untreated well-water, additional risk might result because of microbial or chemical contamination.

The Committee encourages the Agency to consider the many dimensions of their application of the affordibility criterion in the manner described in the arsenic proposal.

4.2.2 Practical Quantitation Level (PQL)

The proposed rule states that the PQL for arsenic is 3 µg/L. In addition, the USEPA's Office of Ground Water and Drinking Water presented to the Science Advisory Board Drinking Water Committee in February, 2000 data that led them to set the PQL at 3 µg/L with acceptance limit of ±30%.

It is not clear to the committee whether the spike tests were conducted in laboratory waters or in natural waters. This is an important issue because the arsenic analytical methods, primarily ICPMS, experiences interference from chloride ion. It is likely that the PQL for arsenic in natural waters may be higher than 3 µg/L. Tables 3 and 4 show the analytical results from five laboratories on arsenic levels in five groundwater samples collected from California, Arizona, and Nevada and one blank sample. The five laboratories used both ICPMS and GFAA methods.

Table 3. Results of Arsenic Analyses in Natural Waters [ICPMS Method]

Sample	Lab 1	Lab 2	Lab 3	Lab 4	Lab 5	Average	Std. Dev.	% RSD
A	<2*	4.0	1.2	3.9	5.6	3.3	1.7	52
B	14.2	12.0	12.9	18.1	11.8	13.8	2.6	19
C	3.18	3.0	1.7	3.9	5.6	3.5	1.4	41
D	2.72	4.0	2.2	5.2	5.8	4.0	1.5	39
E	<2*	2.0	1.6	4.2	4.1	2.8	1.3	45
Blank	<2	<1	<2	<1	<1	-	-	-

*These values were set at their detection limits when calculating the average, standard deviation, and %RSD

While these results were not conducted as part of a formal PQL study, they do suggest that the PQL in natural waters is likely to be greater than 3 µg/L. Considering that the proposed PQL of 3 µg/L is very close to the proposed MCL of 5 µg/L, it seems to the committee that a more thorough assessment of the PQL, and the acceptance criteria at that PQL is warranted. Figure 5 shows a plot of the %RSD versus average concentration for both methods. Clearly, these results question whether an acceptance criteria of ±30% is applicable at 3 µg/L.

Table 4. Results of Arsenic Analyses in Natural Waters [GFAA Method]

Sample	Lab 1	Lab 4	Lab 5	Average	Std. Dev.	% RSD
A	4.02	1.7	4.47	3.4	1.5	44
B	13.42	12.2	13.80	13.1	0.8	6
C	2.08	1.8	2.81	2.2	0.5	23
D	4.47	2.0	2.18	2.9	1.4	48
E	3.83	<1*	3.60	2.8	1.6	56

Blank	<2	<1	<2	-	-	-

*This value was set at its detection limit when calculating the average, standard deviation, and %RSD

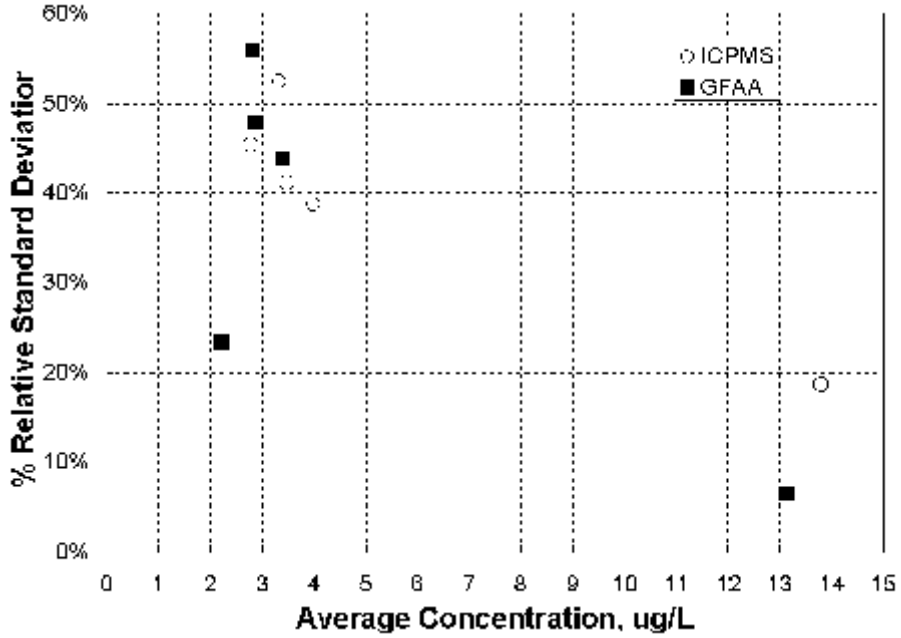
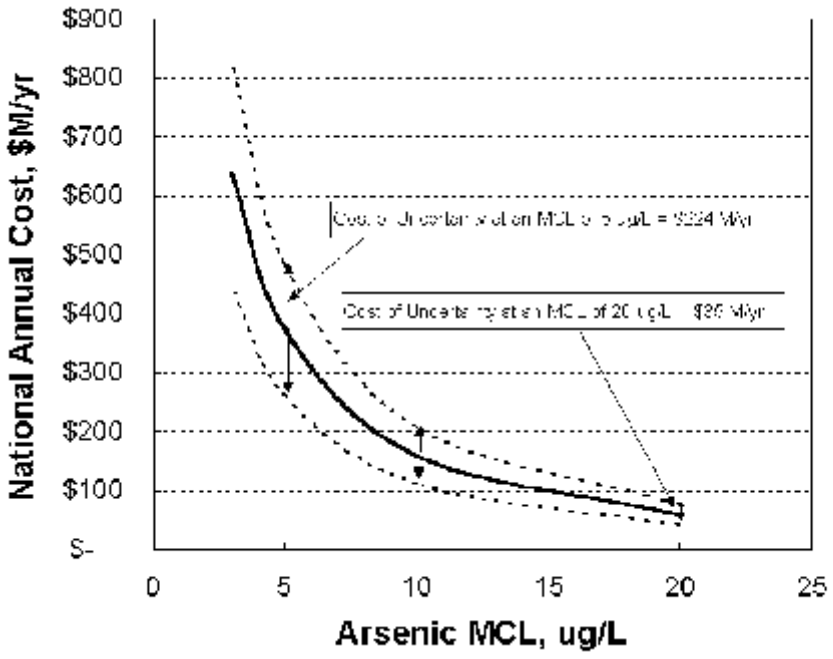


Figure 5. Percent relative standard deviation as a function of average arsenic concentration (ICPMS – 5 measurements/datapoint; GFAA – 3 measurements/data point.

4.3 Need for Performance Data on Arsenic Technologies

The committee believes that there is uncertainty in both the health effects and the limited cost analyses provided to the DWC by EPA. This could result in substantial uncertainty in the final national

cost and benefit estimates for reducing the arsenic MCL from 50 µg/L to 5 µg/L. Further, this uncertainty is substantially greater at low values of the MCL (see the illustration in Fig 6 which uses an uncertainty factor of 30% as an example). As such, it appears that the outcome of mandating such technologies across the country before reliable information on their performance is available will be difficult to predict. The Committee recommends that the Agency consider whether it might be appropriate to gather performance data for technologies identified by their decision tree as it has done in some earlier situations. For example, such a rationale was used in the Information Collection Rule (ICR) which required collection of data on the performance and cost of certain treatment technologies during the Microbial/Disinfection Byproduct regulatory process. These data, which were not available on a national basis, were needed before these treatment technologies were to be implemented by utilities across the country.



It seems to the committee that EPA could consider setting a higher MCL as a first step of the arsenic rule with an announced intention to lower the MCL to its final {DFO} at a future date. During that interval, sufficient data would be collected on the performance and cost of technologies implemented to comply with the interim MCL in those systems needing to reduce levels of arsenic in drinking water. EPA would then have sufficient data to be able to reevaluate the MCL as a second step of the rule.

Figure 6: Cost of a 30% Uncertainty (as an example) in EPA's National Cost Estimate

5.0 CONCLUSIONS

The Committee recognizes that selection of the MCL is within the policy domain of EPA and that it is not just a scientifically derived number. In setting a Maximum Contaminant Level, EPA must consider costs of implementing the rule and the benefits of decreased health risks. Considerable uncertainty exists in the calculation of both costs and benefits for this rule. Even so, it was the unanimous opinion of the DWC that the MCL needs to be ~~significantly~~ reduced from its current level of 50 ug/L. Each member of the DWC has his/her own views about why the MCL should be more or less restrictive.

Uncertainties in the health data exist and cause some to suggest that an even more cautious MCL selection is appropriate while others suggest a higher MCL is warranted because the Agency neglected many cautionary statements provided in the NRC document about the shortcomings of the Taiwanese data for estimating risks in the U.S. The Committee believes that the uncertainties in applying risk estimates from the study population in Taiwan to estimation of cancer and non-cancer risks from arsenic in the U.S. are very large. Some of this concern over the uncertainty could be resolved if the Agency would extend the analysis of the potential effects of the uncertain risk factors, thus following the advice of the NRC to perform additional formal risk assessments on these data that consider how these factors may have modified the responses to arsenic.

When the uncertainties that arise from reliance on the Taiwanese data are combined with the apparent overestimation of the lung cancer risks in the Agency's benefit analysis and the substantive costs of implementing the lowest MCLs considered by EPA the Committee believes that EPA could judge that it has sufficient grounds to consider an alternative MCL for arsenic under the discretionary authority of the 1996 SDWA Amendments. There are technological uncertainties and they impact on implementation costs. These considerations could be addressed by implementing the reduction in a phased manner, that is allow a higher MCL, initially.

The recommendation for a stepwise approach could be supported by the following rationale:

i) Setting the initial MCL at a higher level than the final target level would require utilities with the highest levels to implement arsenic treatment first. This would allow for the gathering of "real life" data on the performance and cost of various technologies for arsenic removal without establishing a regulation that runs the risk of imposing very substantial costs on the nation prior to determining the full impact of doing so.

ii) It is noted that these arsenic treatment systems will utilize the same technologies set as BAT by the EPA, and most of them (such as IX and AA) will produce waters that have arsenic

levels at or less than 3 µg/L virtually all the time. Therefore, if the later rulemaking activity sets a lower MCL, these systems will be able to comply with these lower MCLs.

iii) In addition, the installation of these treatment systems will also allow the EPA and the industry to evaluate the validity of the assumption that the solid residuals from these technologies can be disposed in municipal landfills. This issue has a significant impact on the national cost of an arsenic MCL.

iv) The feasibility of financing, designing, constructing, and commissioning of a large number of treatment systems is in question. A stepped rule will allow for a more practical implementation schedule.

v) Under the assumption of linearity, the efficiency of risk reduction is greater (i.e., the costs per unit risk reduction are lower) at the higher arsenic concentrations, in other words, the first increments of arsenic reduction below 50 µg/L are more cost-effective than further reductions, at least for small systems (Figure 3B). If future research establishes parameters for a sublinear dose-response curve, then the differences in efficiency at the upper ranges of the exposure distribution relative to the lower ranges of the exposure distribution would be even greater than the differences under a linear-dose response curve.

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ATTACHMENT A

A MINORITY REPORT ON ARSENIC IN DRINKING WATER: THE UNIQUE

SUSCEPTIBILITY OF CHILDREN TO ARSENIC

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1

I. *SOME PRINCIPLES OF PEDIATRIC AND DEVELOPMENTAL TOXICOLOGY*.

Some basic principles of pediatric-developmental toxicology are presented below. In the following section**(II)**, the unique susceptibility of young children to arsenic is outlined, within the context, phrased simply, that children are not young adults; differences in diet, metabolism, body weight, variable age groups, consumption of water, toxic effects of metal pollutants in a rapidly growing organism, and exposure estimates per unit of body weight are essential ingredients of risk assessment in children. In brief, determination of safe levels of exposure to arsenic should take into consideration physiological factors that can place the fetus, infant and young child at greater risk of harmful health effects than adults. Differences in size, maturity of biochemical and physiological functions in major body systems, and variation in body composition(water, fat, protein and mineral content) all can modulate the severity of toxicity to any toxicant in a rapidly developing fetus-infant-child, *including arsenic***.** Because newborns are the group most different anatomically and physiologically from adults, they can exhibit the most pronounced quantitative differences in sensitivity and susceptibility to environmental toxicants, including *arsenic*(1-6**).**

Furthermore, uncertainty factors are widely used to establish guidelines for human exposure. This is often accomplished by dividing the no-observed-effect-level(NOEL) by an uncertainty factor of 100 in animal studies. This factor comprises two separate factors of 10-fold each: one allows for uncertainty in extrapolating experimental data to humans; and the other accommodates variation within human populations. To provide added protection during early development, a third uncertainty factor of 10 is applied to the NOEL to develop the RfD. Because there exist uncertainty factors relating to susceptibility and vulnerability during early fetal, neonatal and childhood developmental toxicity, an additional 10-fold factor is used by EPA and FDA when testing data relative to children is incomplete. This is not a new or additional uncertainty factor but an extended application of uncertainty factors *routinely used by agencies of the U.S. Government*(7-9). In risk assessment, when there is some level of uncertainty relating to the overall quality of available data, *an additional factor, typically 3-fold, is included as a "modifying" factor*. In summary, there are unique risks and increased susceptibility of the fetus, young infant and child to damage from environmental chemicals, including arsenic. These risk assessment paradigms are recognized broadly by the U.S. government. Arsenic fits directly into the above paradigms.

II. *THE UNIQUE SUSCEPTIBILITY OF YOUNG CHILDREN TO EXCESSIVE TOXICANT EXPOSURES*:

The NRC/NAS(10) recognized that a margin of safety may be needed when conducting risk assessments of arsenic, because of variations in the sensitivity of individual subpopulations.

Some general concepts followed by specific examples in different organ systems are provided below.

Children are a unique population; and their risks can differ qualitatively and quantitatively from those in adults(10,11) *These differences include organ systems that are primarily affected by arsenic, such as the central nervous system, cardiovascular development, reproductive and developmental organs and cancinogenesis*(10).

Physiologically, respiratory and circulatory flow rates, as well as cellular proliferative rates, in many organs, are greater in children versus adults. From a metabolic standpoint, some enzymatic pathways are more efficient in the young(the P450s peak in adolescence) and others are far less effective in young children, such as glucuronidation. Developmental changes in cell permeability, binding and storage modulate the distribution and excretion of xenobiotics. The amount of water intake(see below) and dietary status differ in young children compared with adults. From an environmental standpoint, living space and habits, specific to neonates and young children, are highly specific for these young age groups. Clearly, variations in chemical sensitivity and exposure exist in children in contrast to adults; and developmental changes from fetal to newborn to postneonatal to adolescence periods are superimposed on genetic and environmental variables in the young child, which are evidently different from those in adults. Moreover, early exposure in infancy to toxicant metals, such as lead(12) or arsenic(13) can lead to latent adverse health effects that become manifest later during adulthood.

Excretory capacity, in relation to the kidney, undergoes a considerable amount of maturation with aging. Renal clearance is reduced at birth and gradually matures over the first few years of life; and similar maturation in the liver, in the metabolism of xenobiotics, also occurs with aging.

In terms of water intake, body mass and cellular proliferation, in the brain, for instance, the differences between young children and adults are marked. 1) *The body surface:body mass ratio declines by about 66% from infancy to the adult years*; 2) Brain growth is extremely rapid in the first two years of life. About 75% of all brain cell types are present by the age of two years; and the brain represents a considerably larger portion of an infant's body mass compared to that in adults. Cerebral blood flow is also far more robust: a ten year-old has a flow rate of about 50L/Kg brain weight compared to about 40L in a 65 year-old adult. Thus, the younger the child, both brain mass and cerebral blood flow are considerably greater in contrast to adult values; 3) *The Tolerance Assessment System(TAS), used by the US EPA, indicates unequivocally that infants and young children consume the highest amount of water per unit body weight during their entire lifetimes.* An

infant, a 1 to 6 year-old, a 7-12 year-old children consume 28 grams of water/Kg body weight/day, 30 grams of water/Kg body weight/day and 17 grams of water/Kg body weight/day, respectively, in contrast to an adult who typically consumes about 10 grams of water/Kg body weight/day. Obviously, the intake of arsenic from drinking water will be greatest within the pediatric age group**(**11**).**

In addition to all the above differences between children and adults, it can be concluded that infants and young children, *in contrast to adults*, have different exposures to toxic metals in water, have different life expectancies, absorb and maintain unique internal doses of a toxic metal from similar external exposures and respond differently and specifically to the same internal dose of a toxic metal.

III. *THE CENTRAL NERVOUS SYSTEM(CNS):*

Development of the human CNS involves the production of 100 billion nerve cells and 1 trillion glial cells(5**).** Once produced, these cells undergo migration, synaptogenesis, selective cell loss and myelination. This progression occurs unidirectionally. Thus, inhibition at one developmental stage can cause alterations to subsequent processes. Developmental stages occur in temporally distinct time frames across different brain regions thereby making the brain heterogeneous in response to agents that interfere with specific processes. Unlike other organ systems, the unidirectional nature of CNS development limits the capacity of brain tissue to compensate for environmentally induced cell loss. Maintenance of this rigid temporal and spatial schedule allows the brain to develop its various functions. It is this developmental complexity that underlies the sensitivity of the CNS to environmental insults and emphasizes the unique characteristics of development which place children at special risk from environmental exposures. In 1984, the US EPA indicated that children may be more susceptible to arsenic-induced CNS damage(14)**.** For example, severe CNS deficits were observed in children exposed as babies to arsenic-contaminated powdered milk formulas. Follow up of these babies into childhood revealed an increased incidence of severe hearing loss, abnormal EEG patterns, and an increased prevalence of mental deficiency, seizures and other indices of severe brain damage.

IV. *THE REPRODUCTIVE SYSTEM:*

Toxicant exposure is known to affect critical events in the development of the reproductive system(15). Once exposure has sufficient influence on essential reproductive events, adult reproductive competency is reduced or abrogated. Critical windows of development are limited temporally and characterized by occurrence of sets of organizational events that constitute periods during which exposure can have effects on later reproductive competency. Environmental exposures can influence fertility to early embryo loss. Although early embryogenesis is a critical target of toxicants,

preconceptional and even postnatal exposures may also adversely affect the reproductive system and progeny outcomes.

V. *THE CARDIOVASCULAR SYSTEM:*

Three to eight weeks following fertilization is the critical time period of organ(heart) formation. At that time, stem cell populations for organ morphogenesis are established and inductive events of differentiation occur(16). During this time, structural defects in the heart can ensue. It is this very narrow time frame when the anlage of the heart is first established. Moreover, later adverse effects can occur as various cell types begin to differentiate.

VI. CARCINOGENESIS:

The relevance of carcinogenesis to at risk children is discussed on pages 5 and 6(Section **VII.4**).

VII. *THE IMPACT OF ARSENIC ON CHILDREN:*

1) The NAS/NRC document on arsenic(10) concluded that the current MCL of 50 ug/L does not achieve EPA's goal for public health protection and, therefore, requires downward revision as promptly as possible. Similarly, Morales, Ryan et al., (13) also concluded that 50 ug/L of arsenic is associated with a substantial increased risk of cancer; and this MCL is not sufficient to protect the public's health. For adults, EPA found that the safe level of arsenic, to avoid non-cancer diseases, is 0.3 ug/kg/day(U.S EPA. IRIS online: Arsenic, inorganic: 4/10/98, 0278, off the internet 5/15/00**).** To extrapolate this value to young children requires dividing the above intake by a factor of at least 6-10(see above and below). Morever, if the daily intake of arsenic by an adult is about 21 ug/day, and the water intake is about two liters, this equals arsenic at a concentration of about 10 ug/L. For Superfund sites of which I am familiar, (Palmerton and Throop, PA and Kellogg, ID), this places arsenic in the category of an hazardous toxicant at Superfund sites for adults, without any consideration for the increased susceptibility of young children. As defined by EPA, any MCL above 5 ug/L is, at the very least, an hazard to human health and even more so for children(see below).

2) In children, the arsenic dose per unit of body weight is about 6-fold times higher than in adults(17). Calderon et al.(17) concluded that the age-dependent difference in arsenic urinary concentrations can be attributed to the higher dose per unit body weight in children versus adults.

3) In a broad range of ages, children do not detoxify arsenic as efficiently as in adults (18, 19). The net result in children is that increased amounts of arsenic are available to produce toxic effects.

4) Toxic exposures to the fetus and in childhood are recognized determinants of cancer in adulthood(20-23); and such periods of latency have been demonstrated for hepatitis B exposure in infancy leading to hepatocellular carcinoma in adults(20). Morever, models exist of multi-step carcinogenesis incorporating initiation and progression to latent expression of disease. Toxicant exposure during conception or pregnancy can provide the initial mutational event that provides increased risk of cancer during adulthood. An adult will be at higher risk for cancer, once a germline alteration occurs; toxicant exposure can lead to somatic alterations postnatally with long latency periods(20-23).

Children have a general sensitivity to carcinogens that can be demonstrated by early biomarkers of cancer; and this may foretell an unique sensitivity in childhood even when cancer latency is long(22,23). It is important to point out that cancer biomarkers in young children vary considerably with ethnicity(22); and this observation may place specific ethnic groups of children at higher risk for developing arsenic-induced cancer as adults(22). Although there is presently an absence of longitudinal studies of excessively exposed young children to arsenic, ultimately leading to cancer in adulthood, the pathophysiological frame work exists in the fetus, infant and young child for such events to occur. Thus, the fetus, infant and young children should be considered to be at increased risk for developing arsenic-induced cancers after long latency periods.

5) To dismiss the Taiwanese data(24) in young and older children in this country is a simplistic approach to this country's pediatric population. The majority report posits that all American children, exposed to arsenic, have a nutritional status that is *complete* compared to the Taiwanese population. "If individuals in the Taiwan endemic zone were at added risk for arsenic effects by virtue of poor nutritional status, then individuals anywhere with this risk factor are of concern(25)." There are about 13 million American children who are living below the poverty line today in the United States(New York Times. 8/13/00) of diverse ethnicity(African-American, Hispanic and Native American children); and these subpopulations of American children, except, perhaps, for selenium, are more likely than not to be in poor nutritional status. Indeed, Smith(26) found the prevalence of skin lesions among men and children in a relatively small population, who had been drinking water containing excessive quantities of arsenic for decades within Northern Chile, was similar to the prevalence of these arsenic induced skin lesions reported from Taiwan and West Bengal(27). However, the North Chilean population was nutritionally sound in contrast to malnutrition reported from Taiwan and West Bengal. Although the sample size was small in the North Chilean population, the findings were robust.

The above reality is especially operative for arsenic and nutritionally at-risk children in America.

Many of the areas of the United States, which contain relatively high-risk fractions of particularly at-risk children, including Native American children, are also those areas where water arsenic levels are high, such as in desert areas of the Southwest. Arsenic-laced water consumption among risk groups in the Western United States would parallel the case for the Taiwanese, even if one were to accept that nutritional deficiencies were pivotal and determinative for carcinogenic and other non-cancer outcomes in the Taiwanese people.

Welch et al.(28) recently summarized data from the United States Geological Survey at an International Conference on arsenic exposure and health effects. Analyses were based upon over 17, 000 analyses of arsenic recorded by the USGS National Water Information System(NWIS). NWIS data revealed that Western areas of the United States have significantly higher rates of exceedences using any standard cut-point for arsenic (current or proposed EPA, current WHO) compared to water supplies in the East. These data are also in agreement with a related survey, namely, the National Arsenic Occurrence Survey(29).

Native American children living in the Western U.S., particularly reservation populations in desert areas of the Southwest are subjected to the poorest and most risk-producing factors for adverse effects of arsenic in America. They have higher rates of poverty and typically have higher rates of nutritional deficiencies in contrast to other demographic and socioeconomic subpopulations in the United States. Furthermore, a number of Native American tribes have contemporary diets that are clinically recognized as predisposing to diverse chronic diseases, for example, cardiovascular and cancer-based adverse health effects. These factors pose additive and, perhaps, synergistic risks together with excessive arsenic intake from water. This is especially relevant to areas of the Southwestern United States.

Ballew(30) recently described data for the Navajo in a "Navajo HANES"(Health and Nutrition Survey) a demographic and ethnic spin-off of the NHANES surveys, similar to the "Hispanic HANES" carried out in the 1980s as an adjunct to the 1976-1980 NHANES II. Navajo diets are typically low in important sources of vitamins and minerals(30), as are the diets of the Hopi and the Pima(31,32).

The U.S. EPA and SAB Committee cannot claim ignorance of the potential consequences of nationally high-risk Native-American children(and adults), because the 1997 Exposure Factors Handbook, widely used by risk assessors in various U.S. regulatory scenarios, includes coverage of this issue of intakes and diets of Native Americans(33). This multi-volume EPA document presents information for Native American tribes based upon data from four of these.

Overall, the SAB Committee and U.S. EPA must address the fact that, when one looks at high

water levels of arsenic that simultaneously serve as a potential water source for nutritionally-deprived and otherwise at risk Native American children and adults(who are also likely to have increased intakes of water arsenic and consume animal herds who also drink arsenic-contaminated water), these populations would be similar to the Taiwanese in terms of exposure and nutrition. The article by Harris and Harper(34) should be consulted to examine the extent to which intakes of toxicant-contaminated media are remarkably different and much higher than non-Native American populations.

My own direct experience as a clinician working with Navajo includes recently published findings that arsenic and other chemical toxicants, in tandem with radionuclides, will, in fact, produce toxic harm in utero and post-natally in Navajo children(35,36). A detailed clinical and risk assessment evaluation of two Navajo sisters, exposed in utero and in early life to arsenic and other toxicants in pit waters was carried out. They were excessively exposed to arsenic during their pastoral family activities of herding the family's sheep on the Navajo reservation in Arizona. The net CNS result was a severe toxic peripheral neuropathy and CNS cortical disease.

Through direct interviews with Navajo family members, it was ascertained that many of the intake parameters(water, in particular), described by Harris and Harper(34) as potentially elevated, were in fact markedly elevated. This Navajo family spent its herding existence within an highly arid environment coming into contact and consuming higher amounts of arsenic contaminated water than typical children or even Native American children, who did not engage in pastoral activity.

In view of the above discussion, it is reasonable to conclude that the subpopulation of American children are at higher risk for arsenic-related disease than others from a nutritional standpoint, if the postulate(relating to malnutrition) is as strongly supported as it is in the majority report.

6) The recent article by Hopenhayn-Rich et al.(37) reported elevated late fetal, neonatal and postnatal mortality in a Chilean town(Antofagasta) with high levels of arsenic in drinking water compared to a control town(Valparaiso), where arsenic levels in drinking water were less than 5 ug/L. Similar results, reported from Bulgaria, including congenital malformations(38), from Texas(39) and from other parts of the United States, including congenital cardiovascular malformations, and spontaneous abortions, collectively support the view of increased susceptibility of the fetus and neonate to arsenic (40-42). Drinking water levels of arsenic decreased in Antofagasta from 1961 on, so did the prevalences in fetal mortality rate, neonatal mortality rate and postnatal mortality rates. In contrast, when arsenic water levels were elevated pre-1961, the combined mortality rate was 68 deaths per 1000 births.

More specifically, these data reflect a dose-response curve that is typically found in the field of toxicology(43-50). From 1974-1977, although mortality rates were still elevated in Antofagasta, a gradual decline in these rates was observed as drinking water concentrations of arsenic decreased from

860 to 110 ug/L. In the period of about 1978-1982, the mortality rates in both towns were similar; but the rate of decline in Antofagasta was far more pronounced over the preceding years than that in Valaparaiso. Moreover, the rate of decline into the 1980s was the most pronounced for postneonatal mortality in Antofagasta, with more gradual reductions in neonatal and late fetal mortality. Arsenic levels in this town were decreased to 40 ug/L from the previous value of 70 ug/L. Statistically, Poisson regression analyses(with relatively few data points) were used to fit the mortality rates as a function of the estimated exposure to arsenic by log-linear models adjusting for location and calendar time(37). Arsenic values for Valparaiso were measured by the Chilean government and the authors; levels less than 5 ug/L were reported. Data collected from water companies during 1990-1994 found that arsenic levels in Valparaiso were below the analytical detection limit of 20 ug/L.

In the report by Hopenhayn-Rich and co-workers(37), data were analyzed in 4-year blocks of time, because there was considerable variation in annual mortality rates. Nonetheless, in the majority report, these originally reported data were analyzed year-by-year; and it was concluded that a dose-response curve was absent. It is scientifically unsound to re-calculate original data by artificially creating unreported data. Using the original data, as reported, analyses were carried out by linear regression, Spearman's rank correlations, and ANOVA. The p values from these three statistical methods ranged from <0.044 to <0.01 thereby indicating a typical toxicological dose-response curve as stated above(Rosen: Unpublished observations).

Hopenhayn-Rich(37) did acknowledge the possibility of confounders in ecologic studies, such as the design of their study. However, the distinct temporal pattern of infant mortality rates in Antofagasta compared to Valparaiso argued strongly against individual-level confounders; and the changes in the arsenic levels in the water was an "indisputable" event. The authors concluded that "the results of this study indicate that exposure to inorganic arsenic from public water supplies may be associated with increased risk of infant mortality. Specifically, these data suggest that arsenic exposure may represent a greater risk for late fetal mortality with lower, but still elevated, risk for neonatal and postneonatal mortality."(37).

The findings of Hopenhayn-Rich(37) are consistent withe the report of Concha et al.(51), which showed that ingested arsenic crosses the placenta during pregnancy, producing fetal exposure, as indexed by levels of arsenic in cord blood. The levels of arsenic in cord blood approached those measured in maternal samples. While this study appeared to show that arsenic metabolites were present, at this time, it cannot be ruled out that these metabolites were toxicologically inconsequential. In fact, these data gain increased support for their toxicological significance from the findings of Hopenhayn-Rich(37), which are consistent with animal studies

summarized in the NAS/NRC report(10). As noted(10), animal species do show reproductive and developmental effects of arsenic evidenced by birth defects, impaired fetal growth, and reduced survival rates for fetal and newborn animals.

Collectively, it can be concluded that the above data indicate that young children are an uniquely susceptible population for adverse health effects of arsenic. Safety information based upon data from adults, in view of all the aforementioned differences between young children and adults, are highly unlikely to effectively protect children, as a subpopulation most at risk. In the interests of public health, the population of the developing fetus, neonate and young infant should be rigorously protected by considerable lowering of the MCL for arsenic to the very lowest level that is analytically reliable. A step-wise "phase-down" of the MCL will not protect this susceptible population.

VIII. *CONCLUSIONS*.

From a public health point of view, establishing new guidelines in drinking water for a potent toxic metal, namely, arsenic, requires protecting the most susceptible population. In this instance, the population includes the developing fetus, neonate, infant and young child. To protect this susceptible population *now*, the MCL for arsenic should be as low as analytically feasible. Any type of "phased-in" approach, above that which is analytically possible, will fail to protect a large population of susceptible young children.

IX. *THE MEDICAL AND PUBLIC HEALTH NEED FOR AN EPA DRINKING WATER HEALTH ADVISORY.*

I strongly endorse the need for the U.S. EPA to issue a health advisory for arsenic in drinking water. I do so within my knowledge of the current data base supporting the need for such an advisory. It is my understanding that EPA has issued such advisories on numerous occasions. These can be documented by anyone on the SAB Committee examining the online IRIS file for the many contaminants contained therein. An explicit section in each of these files refers to health advisories. In my informed opinion, the evidence for the need of such an advisory is compelling, as is my understanding of EPA's requirement to do so.

The evidence that compels such an advisory, particularly for those regions in the United States where water supplies of arsenic are elevated, is clear from the voluminous evidence for arsenic within its toxicological and epidemiological context. This evidence indicates that the current MCL is inadequate; and that currently available science dictates a drastic downward revision. While a substantial revision

must follow along a feasible track for implementation, arsenic does not await imparting toxic effects while various regulatory frameworks become operative. *Children specifically will continue to be exposed while control measures are put into place by EPA.* Therefore, the U.S. EPA must take cognizance of the public health realities–that between on-going intoxication and practical needs for implementation time frames-by using

the advisory as a mechanism of public health awareness and education. The mechanisms for how an advisory is issued are, generally, in place and have been used extensively in the past. No deviance from this process is necessary.

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ATTACHMENT B - Acronyms and Abbreviations

BAT	**Best Available Treatment**
CWS	**Community Water System**
DWC	**Drinking Water Committee**
GFH	**Granular Ferric Hydroxide**
LS	**Lime Softening**
MCL	**Maximum Contaminant Level**
MHI	**Median Household Income**
POE	**Point of Entry**
POTW	**Publically Owned Treatment Works**
POU	**Point of Use**
PQL	**Practical Quantitation Limit**
SAB	**U.S. EPA Science Advisory Board**
SDWA	**Safe Drinking Water Act Amendments of 1996**
TCLP	**Toxicity Characteristic Leaching Procedure**
TDS	**Total Dissolved Solids**

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